Draft Screening Assessment

Alcohols Group

Environment and Climate Change Canada
Health Canada

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Synopsis

Pursuant to section 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of 21 substances referred to collectively under the Chemicals Management Plan as the Alcohols Group. These substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority on the basis of other human health concerns and are listed in the table below.

Based on considerations including common chemical structure, hazard properties, or exposure patterns, the alcohol substances are assessed as different subgroups or individual substances and in different chapters of this report.

Table 1. List of substances evaluated in the Alcohols Group

CAS RN[1]	Domestic Substances List name (common name or abbreviation)	Subgroup name
111-27-3	1-Hexanol	Long-chain alcohols
111-87-5	1-Octanol	Long-chain alcohols
143-08-8	1-Nonanol	Long-chain alcohols
112-30-1	1-Decanol	Long-chain alcohols
112-53-8	1-Dodecanol	Long-chain alcohols
112-72-1	1-Tetradecanol	Long-chain alcohols
36653-82-4	1-Hexadecanol	Long-chain alcohols
67762-30-5[a]	Alcohols, C_{14}-C_{18}	Long-chain alcohols
8027-33-6[a,b]	Alcohols, lanolin (lanolin alcohols)	N/A – individual
124-41-4[b]	Methanol, sodium salt (sodium methanolate)	N/A – individual
67-56-1	Methanol	N/A – individual
71-36-3	1-Butanol	N/A – individual
108-93-0	Cyclohexanol	C6 alcohols
108-11-2	2-Pentanol, 4-methyl (MIBC)	C6 alcohols
77-99-6	1,3-Propanediol, 2-ethyl-2-(hydroxymethyl)- (TMP)	C6 alcohols
108-46-3	1,3-Benzenediol (resorcinol)	Aromatic alcohols
100-51-6	Benzenemethanol	Aromatic alcohols

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	(benzyl alcohol)	
122-97-4	Benzenepropanol	Aromatic alcohols
104-76-7	1-Hexanol, 2-ethyl- (2-ethyl-1-hexanol)	N/A – individual
96-23-1[b]	2-Propanol, 1,3-dichloro- (1,3-dichloro-2-propanol; 1,3-DCP)	N/A – individual
107-18-6[b]	2-Propen-1-ol (allyl alcohol)	N/A – individual

[a] This substance is a UVCB (unknown or variable composition, complex reaction products, or biological materials).
[b] This substance was not identified under subsection 73(1) of CEPA but was included in this assessment as it was considered a priority on the basis of other human health concerns.

The ecological risks of the substances in the Alcohols Group were characterized using the ecological risk classification of organic substances (ERC), which is a risk-based approach that employs multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. Hazard profiles are based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Metrics considered in the exposure profiles include potential emission rate, overall persistence, and long-range transport potential. A risk matrix is used to assign a low, moderate or high level of potential concern for substances on the basis of their hazard and exposure profiles. Based on the outcome of the ERC analysis, the substances in the Alcohols Group are considered unlikely to be causing ecological harm.

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to the environment from the 21 alcohols in this screening assessment. It is proposed to conclude that the 21 substances in the Alcohols Group do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

The long-chain alcohols are industrial chemicals, produced primarily from oleochemical- or petrochemical-based feedstock. According to information submitted in response to a CEPA section 71 survey, three of the long-chain alcohols were manufactured in Canada in 2011 and the substances surveyed were imported into Canada that year. These alcohols are used as raw materials and as surface active agents. They are also used in a range of products available to consumers, such as cleaning agents and cosmetics. Some of the long-chain alcohols may be used as food flavouring agents, as components in the manufacture of food packaging materials, and in incidental additives used in food processing establishments. The long-chain alcohols were not identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity. Given their low hazard profile, the potential risk to human health from the long-chain alcohols is expected to be low.

Alcohols, lanolin, hereinafter referred to as lanolin alcohols, are industrial chemicals used as intermediates or as biodiesel fuel in industrial facilities. According to information submitted in response to a CEPA section 71 survey, this substance was not manufactured in Canada in 2011, but was imported into Canada that year. With respect to products available to consumers, lanolin alcohols are largely used in the formulation of cosmetics, and exposure of the general population is mainly through the dermal route. Lanolin alcohols were not identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity. On the basis of their low hazard to human health, the potential risk to human health from lanolin alcohols is expected to be low.

Methanol, sodium salt, hereinafter referred to as sodium methanolate, is mainly used as a chemical intermediate in the manufacture of specialty chemicals. According to information submitted in response to a CEPA section 71 survey, this substance was not manufactured in Canada in 2011, but was imported into Canada that year. Sodium methanolate is highly reactive with water. This substance was not identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity. The critical effect of sodium methanolate is due to the formation of sodium hydroxide after contact with moisture, resulting in corrosivity to skin and eyes upon direct contact and acute and repeated-dose toxicity by oral, dermal or inhalation routes. On the basis of its minimal exposure to the general population, the potential risk to human health from sodium methanolate is expected to be low.

Methanol is an industrial chemical that is manufactured and imported in large quantities in Canada. Methanol is mainly used in site or industry restricted applications, with the largest market in formaldehyde production. It is used in cosmetics, cleaning agents, adhesives, paint and varnish removers. Methanol may be used as a component in the manufacture of food packaging materials, and is a permitted food additive. Methanol occurs naturally in some foods and alcoholic beverages. This substance has been reviewed by international regulatory agencies. Methanol exposure may arise from oral, inhalation or dermal routes. The critical effects of methanol included developmental effects, such as skeletal malformations in mice and a decrease in brain weight in rats. Considering all available information and routes of exposure of the general population, it is determined that the levels of methanol inhalation exposure from the use of certain paint and varnish removers may pose a health risk. For all other uses of methanol, it is not expected that the general population will be exposed to high levels of methanol under normal conditions; therefore, the potential risks to human health from methanol in uses other than certain paint and varnish removers are expected to be low.

According to information submitted in response to a CEPA section 71 survey, 1-butanol was not manufactured in Canada in 2011, but was imported into Canada that year. 1-Butanol is used in cosmetics, natural health products (NHPs), non-prescription and prescription drugs, cleaning agents, lacquers, automotive care products, and as a solvent in paint and ink products. 1-Butanol occurs naturally in fermentation processes and may also be used as a food flavouring agent and as a component in the

manufacture of food packaging materials. 1-Butanol exposure may occur via the inhalation, oral, or dermal routes. The critical effects of 1-butanol include developmental effects. A comparison of the levels of 1-butanol from use of lacquer with levels associated with health effects results in margins of exposure (MOEs) which are potentially inadequate to account for uncertainties in the health effects and exposure databases.

The C6 alcohols consist of cyclohexanol, 2-pentanol, 4-methyl, and 1,3-propanediol, 2-ethyl-2-(hydroxymethyl)-. According to information submitted in response to a CEPA section 71 survey, the three C6 alcohols were not manufactured in Canada above the 100 kg threshold in 2011, but were imported into Canada that year. These substances are used as solvents in polymer and resin production and in mining. In products available to consumers, they may be used in glaze or ceramic paints, automotive care products, adhesives and sealants, and cosmetics. In addition, the C6 alcohols may be used as a component in the manufacture of food packaging materials and can be present as incidental additives in food processing establishments. They may also be used as food flavouring agents. There is a potential for exposure of the general population to these substances, mainly through dermal absorption from cleaning agents and inhalation. These substances were not identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity. A comparison of the levels of exposure to the C6 alcohols to which the general population may be exposed with levels associated with health effects demonstrates that the MOEs for exposure to cyclohexanol and 1,3-propanediol, 2-ethyl-2-(hydroxymethyl) are considered adequate to address uncertainties in the health effects and exposure databases.

The aromatic alcohols consist of 1,3-benzenediol, benzenemethanol (hereinafter referred to as benzyl alcohol), and benzenepropanol. According to information submitted in response to a CEPA section 71 survey, 1,3-benzenediol and benzyl alcohol were manufactured in Canada in 2011, but benzenepropanol was not reported to be manufactured in Canada above the 100 kg threshold. All three alcohols were imported into Canada.1,3-Benzenediol and benzyl alcohol are used primarily as solvents in polymer and resin production and in mining. In products available to consumers, the aromatic alcohols are used in automotive products, household cleaning products, construction and paint products, cosmetics and NHPs, as well as in non-prescription and prescription drugs. The aromatic alcohols may also be used as food flavouring agents, and benzyl alcohol is a permitted food additive. There is a potential for exposure of the general population to these substances, mainly through dermal and inhalation routes. The critical effects for benzyl alcohol are effects on the nervous system, and those for 1,3-benzenediol and benzenepropanol are reproductive and/or developmental effects. A comparison of the levels of benzyl alcohol for certain cosmetics and NHPs to which the general population may be exposed with levels associated with health effects indicates that the MOE for these exposures are potentially inadequate to account for uncertainties in the health effects and exposure databases. A comparison of the levels of 1,3-benzenediol and benzenepropanol to

which the general population may be exposed with levels associated with health effects shows that the MOEs for exposure to 1,3-benzenediol and benzenepropanol are considered adequate to address uncertainties in the health effects and exposure databases.

1-Hexanol, 2-ethyl, hereinafter referred to as 2-ethyl-1-hexanol, occurs naturally in a number of foods, may be used as a food flavouring agent and as a component in the manufacture of food packaging materials. According to information submitted in response to a CEPA section 71 survey, this substance was not manufactured in Canada in 2011, but was imported into Canada that year. This substance can form during the heat processing of certain foods. These foods include soy sauce and soy-based products, meat and meat products, and foods containing hydrolyzed protein products. The critical health effect for 2-ethyl-1-hexanol was a decrease in serum enzyme levels. A comparison of the levels of 2-ethyl-1-hexanol to which the general population may be exposed with levels associated with health effects indicates that the MOEs are adequate to address uncertainties in the health effects and exposure databases.

2-Propanol,1,3-dichloro-, hereinafter referred to as 1,3-dichloro-2-propanol (1,3-DCP) is an anthropogenic compound. According to information submitted in response to a CEPA section 71 survey, this substance was manufactured in and imported into Canada in 2011. Average and high-end estimates of oral exposure to 1,3-DCP from various food sources produced in 2006 by the Joint (Food and Agriculture Organization/World Health Organization) Expert Committee on Food Additives were used in this assessment. These estimates, which assume a worst-case scenario, are considered to be conservative. A comparison of the levels of 1,3-DCP to which the general population may be exposed from food with levels associated with health effects shows that the MOEs for this substance are considered adequate to address uncertainties in the health effects and exposure databases.

While exposure of the general population to 1,3-DCP is not of concern at current levels, this substance is considered to have a health effect of concern on the basis of its International Agency for Research on Cancer carcinogenic group 2B designation. Therefore, there may be a concern for human health if exposures were to increase. Options are being considered for follow-up activities to track changes in exposure to 1,3-DCP.

2-Propen-1-ol is used in industry in the synthesis of glycerol and other specialty chemicals. According to information submitted in response to a CEPA section 71 survey, 2-propene-1-ol was not manufactured in Canada in 2011, but was imported into Canada that year. It may be used in the manufacture of food packaging materials. This substance occurs naturally in crab meat, rotting mussels, and as a result of the operation of enzymes activated during the crushing of garlic. It can also be formed from the hydrolysis of allyl esters used as flavouring agents in food. Estimates of the exposure of this substance from foods are made from the measured concentration of 2-propen-1-ol in different food categories. A comparison of the levels of 2-propen-1-ol to

which the general population may be exposed with levels associated with health effects shows that the MOEs to this substance are considered adequate to address uncertainties in the health effects and exposure databases.

Considering all the information presented in this draft screening assessment, it is proposed to conclude that methanol, 1-butanol and benzyl alcohol meet the criteria under paragraph 64(*c*) of CEPA as they are entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Additionally, it is proposed to conclude that the remaining 18 substances in the Alcohols Group do not meet the criteria under paragraph 64(*c*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Therefore, it is proposed to conclude that methanol, 1-butanol and benzyl alcohol meet one or more of the criteria set out in section 64 of CEPA and that the remaining 18 substances in the Alcohols Group do not meet any of the criteria set out in section 64 of CEPA.

It is also proposed that methanol meets the persistence but not the bioaccumulation criteria and that 1-butanol and benzyl alcohol do not meet the persistence or bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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1. Introduction

Pursuant to sections 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of Environment and the Minister of Health have conducted a screening assessment of 21 alcohols referred to collectively as the Alcohols Group, to determine whether these substances present or may present a risk to the environment or to human health. These substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority based on other human health concerns (EC, HC [modified 2007]).

The ecological risks of the substances in the Alcohols Group were characterized using the ERC approach (ECCC 2016a). The ERC describes the hazard of a substance using key metrics including mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity, and it considers the possible exposure of organisms in the aquatic and terrestrial environments on the basis of factors including potential emission rates, overall persistence and long-range transport potential in air. The various lines of evidence are combined to identify substances as warranting further evaluation of their potential to cause harm to the environment or as having a low likelihood of causing harm to the environment.

This draft screening assessment includes consideration of information on chemical properties, environmental fate, hazards, uses and exposures, including additional information submitted by stakeholders. Relevant data were identified up to April 2020. Empirical data from key studies, as well as some results from models, were used to reach proposed conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

Some subgroups of the Alcohols Group have been reviewed internationally by the United States Environmental Protection Agency (US EPA), the Organisation for Economic Cooperation and Development (OECD), European Chemicals Agency (ECHA), Joint Food and Agriculture Organization/World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA), and the International Agency for Research on Cancer (IARC). These assessments undergo rigorous review (including peer review) and endorsement. In particular, in the case of OECD assessments, Health Canada and Environment and Climate Change Canada are active participants in this process and consider these assessments to be reliable. The specific international reviews will be referenced as each alcohol subgroup is addressed.

This draft screening assessment was prepared by staff in the CEPA Risk Assessment Program at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological portion of this assessment is based on the ERC document (published July 30, 2016), which was peer reviewed and subject to a 60-day public comment period. The human health section was also subject to external peer review by Dr. R. Manderville (University of Guelph), Dr. P. Autier (iPRI France), and Dr. T. Schulz (University of Tennessee).

While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Environment and Climate Change Canada and Health Canada.

This draft screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific information and incorporating a weight-of-evidence approach and precaution.[2] The draft screening assessment presents the critical information and considerations on which the proposed conclusions are based.

2. Long-chain alcohols

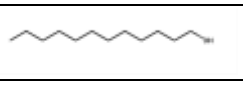
2.1 Substance identity

Information regarding the identity of the long-chain alcohols is summarized in Table 2-1. Common names for these chemicals are also indicated in parentheses, along with their *Domestic Substances List* (DSL) name.

Table 2-1. Substance identity of long-chain alcohols

CAS RN	DSL name (common name)	Molecular formula	Molecular structure	Molecular weight (g/mol)
111-27-3	1-Hexanol	$C_6H_{14}O$		102.2
111-87-5	1-Octanol (caprylic alcohol)	$C_8H_{18}O$		130.2
143-08-8	1-Nonanol	$C_9H_{20}O$		144.3
112-30-1	1-Decanol (capric alcohol)	$C_{10}H_{22}O$		158.3

[2] A determination of whether one or more of the criteria of section 64 of CEPA are met is based on an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other acts.

112-53-8	1-Dodecanol (lauryl alcohol)	$C_{12}H_{26}O$		186.3
112-72-1	1-Tetradecanol (myristyl alcohol)	$C_{14}H_{30}O$		214.4
36653-82-4	1-Hexadecanol (cetyl alcohol)	$C_{16}H_{34}O$		242.4
67762-30-5	Alcohols, C_{14}-C_{18}	UVCB	UVCB	UVCB

Alcohols, C_{14}-C_{18}, are designated as UVCBs.[3] The substance is a mixture of alcohols, where each constituent contains a carbon chain in the indicated length range. The distribution of total carbon count within the range, the chemical structure, and the degree of branching and saturation depend on the manufacturing process (OECD 2006a). Regardless of the inherent variation in the substances of the long-chain alcohols subgroup, they all exhibit similar physical and chemical properties.

2.2 Physical and chemical properties

Measured data are available for the physical and chemical properties of the long-chain alcohols, and the observed ranges are given in Table 2-2. As the carbon number increases in this subgroup of substances, the melting point, boiling point, and log K_{ow} increase, while the vapour pressure and water solubility decrease. Additional physical and chemical properties are presented in ECCC (2016b).

Table 2-2. Ranges of measured physical and chemical properties of long-chain alcohols

Property	Range of values[a,b]
Melting point (ºC)	-50 to +72.5
Boiling point (ºC)	158 to 400
Density (kg/m^3)	800 to 850
Vapour pressure (hPa)	1.22 to 8.2×10^{-8}
log K_{ow} (dimensionless)	2.03 to >7
Water solubility (mg/L)	5900 to 0.001

Abbreviation: K_{ow}, octanol-water partition coefficient
[a] The first value is that of 1-hexanol (which contains 6 carbons) and the other value belongs to the C_{14}–C_{18} alcohols.
[b] OECD 2006a.

2.3 Sources and uses

Some of the long-chain alcohols occur in appreciable quantities in nature. However, these alcohols are manufactured from oleochemical or petrochemical feedstock through a variety of synthetic routes, and production is largely anthropogenic. The process and

[3] UVCB stands for unknown or variable composition, complex reaction products, or biological materials. These materials are derived from natural sources or complex reactions and cannot practicably be synthesized by simply combining individual constituents. A UVCB is not an intentional mixture of discrete substances and is considered a single substance.

feedstock employed govern the linearity, saturation and chain-length distribution of these long-chain alcohols. The total manufacture and import volumes of the long-chain alcohols in 2011 in Canada as reported in response to a CEPA section 71 survey are shown in Table 2-3 (Environment Canada 2013).

Table 2-3. Summary of information on Canadian manufacturing and imports of the long-chain alcohols subgroup submitted in response to a CEPA section 71 survey

Name	Total manufacture (kg)[a]	Total imports (kg)[a]
1-Hexanol	NR	100 000 – 1 000 000
1-Octanol	NA	NA
1-Nonanol	NR	100 000 – 1 000 000
1-Decanol	100 – 1000	1 470 000
1-Dodecanol	1000 – 10 000	1 000 000 – 10 000 000
1-Tetradecanol	NR	1 000 000 – 10 000 000
1-Hexadecanol	1000 – 10 000	1 380 000
Alcohols, C_{14}-C_{18}	NR	284 000

Abbreviations: NR, not reported above the reporting threshold of 100 kg; NA, not included in a survey issued pursuant to section 71 of CEPA.

[a] Values reflect quantities reported in response to a CEPA section 71 survey (Environment Canada 2013), except for 1-octanol, which was not surveyed. See survey for specific inclusions and exclusions (schedules 2 and 3).

The estimated global production volume of these alcohols in the OECD was estimated to be 2.5 million tonnes (OECD 2006a). Over half of the total production volume of long-chain aliphatic alcohols is used as synthetic intermediates, with 65% of this volume used in site-specific applications (OECD 2006a). The substances are extensively applied as production aids, including as surfactants, lubricants, deformers and floating agents, in various manufacturing processes. The remaining half of the production of long-chain alcohols are employed in food packaging materials and as additives in products available to consumers, including personal care products, cleaning products, paints and coatings, and lubricants (OECD 2006a).

The uses of the long-chain alcohols in foods, cosmetics, and natural health products (NHPs) in Canada are summarized in Table 2-4 to

Table 2-6. Long-chain alcohols not included in the tables had no identified uses.

Table 2-4. Possible uses for long-chain alcohols in foods in Canada[a]

Alcohol	Food packaging materials	Incidental additives[b]	Food additives	Food flavouring agents	Potential for exposure
1-Hexanol	No	No	No	Yes	Yes
1-Octanol	No	No	No	Yes	Yes
1-Nonanol	No	No	No	Yes	Yes
1-Decanol	No	Yes (cleaner followed by potable water rinse)	No	Yes	Yes
1-Dodecanol	Yes (adhesives, meat casings, colour concentrates)	No	No	Yes	Yes
1-Tetradecanol	No	Yes (hand rinse)	No	Yes	Yes
1-Hexadecanol	Yes (paperboard, aluminum containers)	No	No	Yes	Yes
Alcohols, C_{14}-C_{18}	Yes (paperboard)	No	No	No	No

[a] Personal communication, email from Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2016, and December 18, 2017; unreferenced.
[b] While not defined under the *Food and Drugs Act* (FDA), incidental additives may be regarded, for administrative purposes, as those substances which are used in food processing plants and which may potentially become adventitious residues in foods.

Table 2-5. Uses for long-chain alcohols in Canada in cosmetics[a,b]

Alcohol	Number of cosmetic products in which substance is found	Product and maximum concentration (wt %)
1-Octanol	7 products	Skin products / 1% Styling product / <0.1%
1-Decanol	4 products	Skin products / 10% Styling product / <0.1% Makeup / <3%
1-Dodecanol	510 products	Skin products / 30% Hair products / 30% Bath products / 3% Toothpaste / 10%
1-Tetradecanol	936 products	Skin products / 30% Hair products / 30%

		Bath products / 3% Makeup / 10%
1-Hexadecanol	12149 products	Adhesives / 100% Antiperspirant / 100% Bath products / 30% Breath freshener / 100% Cleanser / 100% Hair products / 100% Makeup / 100% Massage product / 10% Mouthwash / 10% Skin products / 30% Nail products / 100%

[a] Based on notifications submitted under the *Cosmetic Regulations* to Health Canada. Personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 19, 2016; unreferenced.

[b] None of the substances are included on the Cosmetics Ingredient Hotlist. The List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply the Hotlist), is an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances may contravene the general prohibition found in section 16 of the *Food and Drugs Act* (F&DA) or may contravene one or more provisions of the *Cosmetic Regulations*. Section 16 of the F&DA states that "No person shall sell any cosmetic that has in or on it any substance that may cause injury to the health of the user." In addition, the Hotlist includes certain substances that may make it unlikely for a product to be classified as a cosmetic under the F&DA.

Table 2-6. Uses for long-chain alcohols in Canada in natural health products[a]

Alcohol	NHPID/ LNHPD[b]	Sub-category/comments (*if applicable*)
1-Hexanol	Yes/No	Non-medicinal role for oral use as flavour enhancer
1-Octanol	Yes/No	Non-medicinal role for oral use as flavour enhancer
1-Nonanol	Yes/No	Non-medicinal role for oral use as flavour enhancer
1-Decanol	Yes/No	Non-medicinal role for oral use as flavour enhancer
1-Dodecanol	Yes/Yes	Non-medicinal role for topical or oral use as emulsion stabilizer, flavour enhancer, fragrance ingredient, skin-conditioning agent - emollient, surfactant - foam booster, viscosity increasing agent - aqueous, or viscosity increasing agent – nonaqueous Present in currently licensed NHPs
1-Tetradecanol	Yes/Yes	- Non-medicinal role for use as emulsion stabilizer, flavour enhancer, fragrance ingredient, skin-conditioning agent - emollient, surfactant - foam booster, viscosity increasing agent - aqueous, or viscosity increasing agent - nonaqueous Present in currently licensed NHPs
1-Hexadecanol	Yes/Yes	- Non-medicinal role for use as emollient, emulsion stabilizer, opacifying agent, plasticizer, stiffening agent, surfactant – emulsifying agent, or thickening agent Present in currently licensed NHPs

Abbreviations: NHPID, Natural Health Products Ingredients Database; LNHPD, Licensed Natural Health Products Database

[a] Personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 26, 2016; unreferenced.

Long-chain alcohols occur as formulants in pest control products in Canada (PMRA 2010).

2.4 Environmental fate and behaviour

2.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), long-chain alcohols are not expected to persist in air, water, sediment, or soil.

2.4.2 Potential for bioaccumulation

On the basis of log K_{ow} values of between approximately 5 and 7 and estimated bioconcentration factors ranging from approximately 6000 to 40 000 L/kg (ECCC 2016b), 1-dodecanol, 1-tetradecanol, 1-hexadecanol and alcohols, C_{14}-C_{18} are expected to bioaccumulate in organisms. However, the potential for these substances to bioaccumulate in organisms is likely lower than estimated because of the metabolic

breakdown of these alcohols. Given their low log K_{ow} and low bioconcentration factors (ECCC 2016b), the other long-chain alcohols are not expected to significantly bioaccumulate in organisms.

2.5 Potential to cause ecological harm

2.5.1 Characterization of ecological risk

The ecological risks of the long-chain alcohols have been characterized using the ecological risk classification of organic substances (ERC) approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profiles for the long-chain alcohols and the hazard, exposure, and risk classification results are presented in ECCC (2016b).

The hazard and exposure classifications for the long-chain alcohols are summarized in Table 2-7.

Table 2-7. Ecological risk classification results for the long-chain alcohols

Substance	ERC hazard classification	ERC exposure classification	ERC risk classification
1-Hexanol	low	low	low
1-Octanol	low	low	low
1-Nonanol	low	low	low
1-Decanol	low	low	low
1-Dodecanol	low	low	low
1-Tetradecanol	moderate	low	low
1-Hexadecanol	moderate	low	low
Alcohols, C_{14}-C_{18}	moderate	low	low

On the basis of low hazard and low exposure classifications according to information considered under ERC, 1-hexanol, 1-octanol, 1-nonanol, 1-decanol and 1-dodecanol were classified as having a low potential for ecological risk. It is therefore unlikely that these substances are resulting in concerns for the environment in Canada.

1-Tetradecanol, 1-hexadecanol, and alcohols, C_{14}-C_{18} were classified as having moderate hazard potential according to information considered under ERC because of a moderate potential to cause adverse effects in aquatic food webs given their bioaccumulation potential. However, 1-tetradecanol, 1-hexadecanol, and alcohols, C_{14}-C_{18} were classified as having low exposure potential and therefore an overall low potential for ecological risk. It is therefore unlikely that these substances are resulting in concerns for the environment in Canada.

2.6 Potential to cause harm to human health

2.6.1 Exposure assessment

2.6.1.1 Environmental media and food

The long-chain alcohols have a range of values for water solubility and vapour pressure. Fugacity modelling shows that the predicted environmental fate of substances in this subgroup depends on the type of release. When released to water, chain lengths C_{10} and above are predicted to partition into sediment. When alcohols are released to air, for chain lengths C_{14} and above, less than half of the alcohols ultimately present in the environment can be found in air (OECD 2006a). The long-chain alcohols are not expected to be present in environmental media at significant concentrations because of their low environmental persistence.

As shown in Table 2-4, long-chain alcohols may be used as food flavouring agents, components in the manufacture of food packaging materials and incidental additives used in food processing establishments. As the long-chain alcohols are considered to be of low hazard potential, quantitative estimates of dietary exposure of the general population were not derived.

2.6.1.2 Exposure to products available to consumers

The long-chain alcohols are present in many products available to consumers including cosmetics and cleaning agents. The most frequently used alcohols comprise the longer chains (C_{10}-C_{18}) of carbon. As the long-chain alcohols are considered to be of low hazard potential, quantitative estimates of exposure of the general population were not derived.

2.6.2 Health effects assessment

The long-chain alcohols have been reviewed internationally (OECD 2006a, b; US EPA 2006), and these reports were used to inform the health effects characterization in this assessment. A literature search was conducted for new data from 2006 up to August 2021, and no new studies that could result in a different health effects characterization from that of OECD (2006 a,b) and US EPA (2006) assessments were identified.

The OECD reviewed the group of C_6-C_{22} long-chain alcohols (OECD 2006a). In addition, separate human health and ecological risk assessment documents available for individual or groups of these substances were considered. These include assessments of 1-hexanol (AGDH 2017a), 1-octanol (AGDH 2017b; Bevan 2001; US EPA 2006), 1-hexanol, 2-ethyl (Bevan 2001), 1-nonanol (Bevan 2001), 1-decanol (Bevan 2001; US EPA 2006a), 1-dodecanol (OECD 2006a; MAK 2016; Bevan 2001), 1-tetradecanol (Bevan 2001) and 1-hexadecanol (AGDH 2017c; Bevan 2001).

The OECD (2006a) concluded that the family of long-chain alcohols are of low order of toxicity following acute or repeated-dose oral, dermal or inhalation exposure. There is very low potential of bioaccumulation of the parent alcohols or their metabolites as they

are efficiently metabolized by the body (OECD 2006a). These substances do not pose a hazard to human health for carcinogenicity, genotoxicity, reproductive toxicity or developmental toxicity (OECD 2006a; US EPA 2006).

Also, no signs of toxicity were observed after inhalation exposure to long-chain alcohols (OECD 2006a; US EPA 2006).

Subchronic repeated-dose studies for long-chain alcohols have shown low order toxicity with typical subchronic no-observed-adverse-effect levels (NOAELs) ranging from 200 to > 1000 mg/kg bw/day (OECD 2006a). The NOAELs at the lower end were not associated with any adverse effects, and the only findings included reversible local irritation of skin or eye in male and female rats or mice (OECD 2006a; US EPA 2006).

The primary effects following acute or subchronic exposure to a variety of long-chain alcohols have been reported as mild or local irritation of the skin or eyes following very high doses in laboratory animals. Also, repeated-dose studies showed that the long-chain alcohols do not cause sensitization and do not have the potential to cause neurotoxicity (OECD 2006a; US EPA 2006).

The available data in these international assessments show that exposure to long-chain alcohols via the oral, dermal or inhalation route does not produce adverse systemic effects in laboratory animals. There is no indication that long-chain alcohols cause carcinogenicity, genotoxicity, neurotoxicity or reproductive or developmental toxicity in animals (OECD 2006a; US EPA 2006).

2.6.3 Characterization of risk to human health

Exposure of the general population to long-chain alcohols through environmental media, food, or the use of products available to consumers may be expected. However, because of their low toxicity, the potential risks to human health from exposure to these substances are considered to be low (OECD 2006a; US EPA 2006).

3. Lanolin alcohols

3.1 Substance identity

Information regarding the identity of lanolin alcohols is summarized in Table 3-1. This substance is also known by the common names sheep alcohol and wool alcohol.

Table 3-1. Substance identity of lanolin alcohols

CAS RN	DSL name (common name)	Chemical structure	Mean molecular weight (g/mol)
8027-33-6	Alcohols, lanolin (lanolin alcohols)	Varied composition and structure (75% sterols and triterpene alcohols; also branched and unbranched aliphatic alcohols)	370 (of all alcohols in this substance)

Lanolin alcohols are primarily (75%) composed of sterols and triterpene alcohols, with cholesterol forming the highest individual component (36%), followed by the tetracyclic triterpenoids lanosterol and agnosterol and their derivatives. The sterols in lanolin alcohols are similar to the physiological lipids in the stratum corneum (Imperial Oel 2017).

Lanolin alcohols are designated as UVCB. They are a mixture of alcohols that all exhibit similar physical and chemical properties, low toxicity, and environmental effects. These substances are produced by heating lanolin with water and separating the lanolin acids component of the mixture. In cosmetic products, they are mostly used in acetylated form.

3.2 Physical and chemical properties

Measured values for the physical chemical properties of lanolin alcohols are given in Table 3-2 (O'Neil 2006; ECHA 2017j). Additional physical and chemical properties data are presented in ECCC 2016b.

Table 3-2. Physical and chemical properties of lanolin alcohols

Property	Range of values[a]
Melting point (°C)	45–80
Boiling point (°C)	> 220 to < 420
Density at 20ºC (g/cm^3)	0.935
log K_{ow} (dimensionless)	8.739
Water solubility (mg/L)	0.21
Vapour pressure at 20 °C (Pa)	360

[a] ECHA 2017j

3.3 Sources and uses

Lanolin alcohols are naturally derived substances obtained from the hydrolysis of lanolin (which also produces lanolin acid), a derivative of the fat-like sebaceous secretion of sheep (Cosmetics Info 2016). This process produces anhydrous lanolin, which includes fatty alcohols and fatty acids as well as lanolin alcohols. They are also called wool wax because they aid sheep in shedding water from their coats (Rudner et al. 1973; Rudner et al. 1975).

According to information submitted in response to a CEPA section 71 survey, lanolin alcohols were not manufactured in Canada in 2011, but 1000 kg to 10 000 kg were reported to be imported into Canada that year (Environment Canada 2013).[4]

[4] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

In industry, lanolin alcohols are used as chemical intermediates in the manufacture of textiles, leathers, or fur, and as biodiesel fuels. As emollients that bind well with water (Ngan 2002), lanolin alcohols are largely produced for use in the manufacturing of pharmaceutical and cosmetic products (Environment Canada 2012). Lanolin alcohols are not included on the Cosmetic Ingredient Hotlist. Notifications submitted under the *Cosmetic Regulations* to Health Canada indicate that they are used in certain cosmetic products in Canada. Their uses are summarized in Table 3-3. They are also found in pest control products in Canada as formulants (PMRA 2010). Lanolin alcohols have been used in one skin cream categorized as a natural health product (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated April 30, 2021; unreferenced). Lanolin alcohols have not been identified as being used as components in the manufacture of food packaging materials or as incidental additives used in food processing establishments, and they are not permitted food additives in Canada (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2017; unreferenced).

Table 3-3. Uses for lanolin alcohols in Canada in cosmetics

Total number of products	Categories of products	Highest concentration (weight %)
515	Hair care	30
	Antiperspirant	10
	Bath product	10
	Moisturizer and exfoliant	10
	Massage product	30
	Makeup (eyes/lips)	3 /10

3.4 Environmental fate and behaviour

3.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), lanolin alcohols are not expected to persist in air, water, soil, or sediment.

3.4.2 Potential for bioaccumulation

Although the log K_{ow} value for lanolin alcohols is high (approximately 8), the bioconcentration factor for this substance is low. As a result, this substance is not expected to significantly bioaccumulate in organisms (ECCC 2016b).

3.5 Potential to cause ecological harm

3.5.1 Characterization of ecological risk

The ecological risks of lanolin alcohols have been characterized using the ecological risk classification of organic substances (ERC) approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for lanolin alcohols, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

Lanolin alcohols were classified as having a high hazard potential according to information considered under ERC due to structural alerts from the OECD toolbox (LMC 2017), identifying these substances as potentially having estrogen-binding potential and a reactive mode of action. However, on the basis of their low exposure potential, it is unlikely that these substances are resulting in concerns for the environment in Canada.

3.6 Potential to cause harm to human health

3.6.1 Exposure assessment

Consumers will likely not be exposed to lanolin alcohols through release to the environment via various waste streams. Due to their high boiling point and low volatility, they are not likely to be present in the atmosphere in any appreciable amount. In addition, because of their insolubility in water, wastewater is not likely to be a source of exposure.

Lanolin alcohols are found to varying degrees in products available to consumers. However, the majority of consumer uses are cosmetics or as ingredients in natural health products. The use of lanolin alcohols in cosmetics is expected to result in dermal exposures. Due to the low volatility and nature of the products, inhalation exposure and ingestion of lanolin alcohols are not likely. Lanolin alcohols are not used in food applications; therefore, exposure from food is not expected.

3.6.2 Health effects assessment

There are no international assessments for this substance. Therefore, lanolin alcohols were not identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity.

The primary health effect of lanolin alcohols is expected to be dermatitis in individuals with allergies to wool or lanolin. The CIR Expert Panel reported that no adverse effects of lanolin alcohols have been reported following acute or repeated exposure in experimental animals or human volunteers, further concluding that, on the basis of the

available data, lanolin alcohols and their derivatives were safe for use in cosmetics in humans (CIR 2005).

In a developmental toxicity study, gavage exposure of rats to lanolin alcohols at 0, 100, 300, or 1000 mg/kg bw/day on GD 5 to 19 did not cause any maternal or developmental effects (ECHA 2013).

3.6.3 Characterization of risk to human health

Although there are potential exposures, available human and animal data do not indicate adverse effects from exposure to lanolin alcohols. Accordingly, the potential risk to human health from lanolin alcohols is considered to be low.

4. Methanol, sodium salt (sodium methanolate)

4.1 Substance identity

This substance is commonly referred to as sodium methanolate. Information regarding the identity of sodium methanolate is summarized in Table 4-1 (PubChem2004-).

Table 4-1. Substance identity of sodium methanolate

CAS RN	DSL name (common names)	Molecular formula	Molecular structure	Molecular weight (g/mol)
124-41-4	Methanol, sodium salt (sodium methanolate; sodium methoxide)	CH_3ONa		54.024

4.2 Physical and chemical properties

Measured values for the physical and chemical properties of sodium methanolate are given in Table 4-2 (PubChem2004- ; ChemIDplus 2017). Additional substance-specific physical and chemical properties are presented in ECCC (2016b).

Table 4-2. Physical and chemical properties of sodium methanolate

Melting point (ºC)	Density (g/cm^3)	log K_{ow} (dimensionless)	Vapour pressure (mm Hg)	Auto-ignition temperature (ºC)
>127	1.3	_3.180	4.79×10^{-6}	50–60

Sodium methanolate is very reactive with water, with which it forms caustic sodium hydroxide and methanol in a highly exothermic reaction.

4.3 Sources and uses

According to information submitted in response to a CEPA section 71 survey, sodium methanolate was not manufactured in Canada in 2011, but was imported into Canada in quantities of between 1000 kg and 10 000 kg that year (Environment Canada 2013).[5]

The majority of sodium methanolate produced in industry is used as a solvent and chemical intermediate in the manufacture of bulk, large-scale and specialty chemicals, including petroleum products. It is also used as a trans-esterification reagent in the manufacture of pharmaceuticals, food products, and biodiesel fuels (BASF 2012). According to information submitted in response to a CEPA section 71 survey, sodium methanolate was used as an intermediate in the manufacturing of chemicals in cosmetic products, cleaning and furnishing care products, laundry and dishwashing material, pet care products, and automotive care products. Due to its high reactivity and exothermic reaction with water, sodium methanolate is not expected to be present in an appreciable amount in final products available to consumers.

In Canada, sodium methanolate may be used as a component in polyethylene-based food packaging materials with no direct food contact. Exposure from food is therefore not expected (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 2016; unreferenced). There is no information available indicating any products available to consumers as containing sodium methanolate as an ingredient.

4.4 Environmental fate and behaviour

4.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), sodium methanolate is modelled to have a long half-life (approximately 415 hours) in air. However, given the reactivity of sodium methanolate with water and atmospheric moisture, the actual half-life of the substance in air is expected to be lower. Sodium methanolate is not expected to persist in water, soil, or sediment (ECCC 2016b).

4.4.2 Potential for bioaccumulation

Given its low log K_{ow} and low bioconcentration factor (ECCC 2016b), sodium methanolate is not expected to significantly bioaccumulate in organisms.

[5] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

4.5 Potential to cause ecological harm

4.5.1 Characterization of ecological risk

The ecological risk of sodium methanolate has been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for sodium methanolate and the hazard, exposure, and risk classification results are presented in ECCC (2016b).

On the basis of low hazard and low exposure classifications according to information considered under the ERC, sodium methanolate was classified as having a low potential for ecological risk. It is unlikely that this substance is resulting in concerns for the environment in Canada.

4.6 Potential to cause harm to human health

4.6.1 Exposure assessment

Sodium methanolate is highly reactive and any residual material left in the manufacturing process will react with water to produce methanol and sodium hydroxide in aqueous solution.

Sodium methanolate is not an ingredient in any Canadian products available to consumers. There are also no routine releases of sodium methanolate into wastewater or air, and any methanol by-products of sodium methanolate use are burned in a flare (OECD 2006b). If releases were to occur, the substance would be immediately hydrolyzed to methanol and sodium hydroxide upon exposure to the environment (PubChem2004-).

Exposure to sodium methanolate via environmental media is not expected to occur.

Overall, exposure of the general population to sodium methanolate is not expected.

4.6.2 Health effects assessment

Sodium methanolate has been reviewed internationally, and that review has been used to inform the health effects characterization in this assessment (OECD 2006b). It was not identified as posing a hazard to human health based on carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity classifications by other national or international agencies. This chemical was reported to be a low priority for further work (OECD 2006b) because of the unlikely exposure of the general population to this substance under normal conditions. The critical effect of sodium methanolate is due to the formation of sodium hydroxide after contact of sodium methanolate with

moisture, resulting in corrosivity to skin and eyes upon direct contact and acute and repeated-dose toxicity by oral, dermal, or inhalation routes. Further investigation of health effects is not warranted at this time given the reactivity of this substance to moisture and the low expected exposure of the general Canadian population.

4.6.3 Characterization of risk to human health

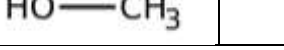
Due to its high reactivity with water and exothermic reaction, sodium methanolate is not expected to be present in an appreciable amount in products available to consumers or in the environment. Overall, exposure of the general population to sodium methanolate is not expected and as a result, the potential risk to human health is considered to be low.

5. Methanol

5.1 Substance identity

Methanol, commonly known as methyl alcohol or wood alcohol, occurs both naturally and anthropogenically. Information regarding the substance identity of this alcohol is summarized in Table 5-1 (ChemID 2017).

Table 5-1. Substance identity for methanol

CAS RN	DSL name	Molecular formula	Molecular structure	Molecular weight (g/mol)
67-56-1	Methanol	CH_4O		32.04

Methanol is miscible with water at all ratios, but also soluble in many other organic solvents.

5.2 Physical and chemical properties

Measured physical and chemical properties of methanol are given in Table 5-2 (ChemIDplus 2017). Additional substance-specific physical and chemical properties are presented in ECCC (2016b).

Table 5-2. Relevant measured physical and chemical properties of methanol

Melting point (°C)	Boiling point (°C)	log K_{ow} (dimensionless)	Water solubility (mg/L)	Vapour pressure (Pa)
−98	65	−0.82 to −0.64	miscible	12 790 at 20 °C

Methanol is degraded by sunlight to produce carbon dioxide and water. Its half-life in the troposphere is estimated to be about 17 to 18 days (OECD 2004c). Methanol is expected to volatilize from water surfaces. Estimated volatilization half-lives for a model river and model lake are 4.6 days and 35 days, respectively (PubChem 2021).

5.3 Sources and uses

Methanol is a naturally occurring substance commonly produced in anaerobic environments by bacteria. As a result, the atmosphere contains a small amount of methanol vapour. Worldwide urban air levels of methanol have been reported to range from 1.05×10^{-5} to 13.1×10^{-5} mg/L (OECD 2004c,d).

In humans, methanol also occurs naturally *in vivo* as a metabolic product. Consumption of fruits, vegetables, and alcoholic beverages has been shown to increase background blood methanol levels. In healthy humans, blood methanol concentrations are found to range from 0.25 mg/L to 5.2 mg/L (IPCS 1997b). The US EPA estimates that 2.5 mg/L represents the high end of blood methanol levels in the average population (IRIS 2013).

Production of methanol is predominantly from anthropogenic sources. Domestic annual production is estimated to range from 600 000 to 700 000 tonnes, but this only accounts for a small fraction of the global manufactured volume (CERI 2016). Canada also exports an additional 250 000 tonnes of methanol per year to the United States and imports approximately the same quantity from the United States for various applications (CERI 2016).

Methanol is a key component in the synthesis of more complex chemicals and is therefore mainly used in site or industry restricted applications (Merck 2010, Methanol Institute 2021). The largest market for methanol is in the production of formaldehyde. The current increase in methanol demand is driven largely by emerging energy applications, which now collectively account for 40% of methanol consumption. These uses encompass gasoline blending, dimethyl ether (DME) and methyl tert-butyl ether production, and direct use as biofuel.

Another application of methanol is in wastewater treatment. Facilities utilize bacteria to denitrify the water prior to discharge to prevent effluent from triggering damaging algae blooms downstream. Denitrification is done under anaerobic conditions, and methanol is added as a biodegradable carbon source to accelerate bacterial activity (Murphy 2009).

Uses of methanol in cosmetics, foods and NHPs in Canada are summarized in Table 5-3. Cosmetics for sale in Canada containing an amount of methanol equal to or greater than 5 mL must be packaged in a child-resistant container in accordance with section 15.2 of the *Cosmetic Regulations* and must carry certain cautionary statements on the label in accordance with section 24 of the *Cosmetic Regulations*. Notifications submitted under the *Cosmetic Regulations* to Health Canada indicate that methanol is used in a total of 27 cosmetic products in Canada. Notifications for two of these products show concentrations up to 3% w/w, with the remaining products indicating methanol content below 0.3% w/w (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 27, 2016). All of these cosmetic products have topical uses and are applied dermally.

Table 5-3. Possible uses of methanol in cosmetics, foods and NHPs[a] in Canada

Use groups	Uses / wt % methanol	Notes
Cosmetics	Hair products / 3% Makeup / 3% Skin moisturizer / 0.1%	In 27 products
Foods and food packaging materials	Printing inks Polymer materials Food additive	Has potential for direct food contact and human exposure
NHPs	Solvent	Listed in the NHPID Present in currently licensed NHPs

Abbreviations: NHPID, Natural Health Products Ingredients Database

[a] Personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 26, 2016; unreferenced.

Methanol and ethyl alcohol denatured with methanol are permitted food additives, used as solvents in a limited number of foods as prescribed in the *List of Permitted Carrier or Extraction Solvents* (Health Canada 2016b), incorporated by reference into its respective Marketing Authorization issued under the *Food and Drugs Act.* Methanol may also be used as a component in the manufacture of various polymer-based food packaging materials (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated December 2016; unreferenced).

Methyl alcohol is listed in the United States Pharmacopeia, with a caution indicating that it is poisonous, with a limit of not more than 200 µL/L., It is one of the organic impurities listed in the Dehydrated Alcohol monograph, as well as being categorized as a Class 2 solvent in the Residual Solvents general chapter. Residual solvents are solvents that should be limited in drug substances, excipients, dietary ingredients, and official products because of the inherent toxicities – with a permitted daily exposure of 30.0 mg/day and a concentration limit of 300 ppm (ICH 2016). Fifty-seven non-prescription drugs list methanol as a non-medicinal ingredient. Seven of these products were discontinued as of 2014 and are unlikely to be present on the market. None of the products list methanol as an active ingredient, suggesting that the substance is present in residual trace amounts left from synthesis, extraction, or other production steps (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 26, 2016; unreferenced). Methanol is also used as an ingredient in coatings of tablets reported as NHPs. This coating is sprayed on tablets and the methanol evaporates after drying (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated June 4, 2021; unreferenced).

Methanol is a formulant in pest control products in Canada (personal communication, email from the Pest Management Regulatory Agency, Health Canada, to the Risk Management Bureau, Health Canada, dated September 2017; unreferenced).

Applications of methanol in products available to consumers stem from the miscibility, volatility, and low melting point of the substance. Methanol is formulated as both a liquid and an aerosol cleaner. The percent concentration varies depending on the intended application, with concentrations ranging from trace to 5% w/w in products meant for frequent inside-the-home use (e.g., floor cleaners, wipes, window cleaners, lens cleaners) (MSDS 2015g).

Paint and varnish removers which contain methanol can be divided into groups which contain methylene chloride (MSDS 2013a, 2015hi,j, 2018b, 2019a,b) and those with other volatile solvents (MSDS 2016c, 2018a). The paint and varnish removers with methylene chloride contain between < 5% w/w and 26% w/w methanol, while those with other solvents contain between < 5% w/w and 35% w/w of methanol. These products are suggested for both interior and exterior use on a variety of surfaces, including wood, ceramics, enamel, metal, and masonry. They can be used to remove oil, latex, and epoxy paints.

Home maintenance products containing the highest methanol concentration by weight are de-icing agents. Methanol is present at up to 75% in de-icing formulations, all of which are intended to be used outside the home (MSDS 2013b).

Methanol is also commonly added to various arts and crafts products. Modelling glues and lacquer thinners are typically under 10% w/w methanol. However, model engine and cooking fuels contain methanol at concentrations of up to 75% w/w (MSDS 2016a).

Domestically available windshield washer fluid is found to contain methanol at concentrations of up to 80% w/w, and some gasoline antifreeze products are reported to be almost entirely methanol (90% to 100% w/w) (MSDS 2014f). Methanol is also added to fuel enhancers to increase the octane number of gasoline/diesel and is sold in cleaners for automotive parts. Formulations for these two applications include the substance at concentrations ranging from less than 5% w/w to 100% w/w (MSDS 2011b, 2014g, 2015f).

5.4 Environmental fate and behaviour

5.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), methanol is expected to persist in air, but is not expected to persist in water, sediment or soil.

5.4.2 Potential for bioaccumulation

Given its low log K_{ow} and low bioconcentration factor (ECCC 2016b), methanol is not expected to significantly bioaccumulate in organisms.

5.5 Potential to cause ecological harm

5.5.1 Characterization of ecological risk

The ecological risk of methanol has been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for methanol, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

According to information considered under ERC, methanol was classified as having a high exposure potential on the basis of a critically long half-life in air and large use quantities. Although the current use patterns result in a high exposure potential, considering its low hazard potential, methanol is unlikely to be resulting in concerns for the environment in Canada.

5.6 Potential to cause harm to human health

5.6.1 Exposure assessment

5.6.1.1 Environmental media and food

There is a potential for methanol to be present in water and air. As noted in section 6.2, methanol has an estimated half-life of 18 days in the troposphere. Based on level III fugacity model calculations, 73% of environmental methanol is distributed to air and 16% to water (OECD 2004c,d).

Estimates of inhalation exposure to methanol are derived using indoor air monitoring data from four Canadian cities. Bari et al. (2015) report on a recent Health Canada study to measure seasonal variations in methanol, in both residential indoor and outdoor environments in Edmonton, Alberta (Health Canada 2013). Indoor residential and outdoor air monitoring studies were also recently performed in four Canadian cities (Health Canada 2010a, 2010b, 2012, 2013). The geometric mean, arithmetic mean, 5th percentile (P5), and 95th percentile (P95) concentrations from sampling over 24-hour periods are given for winter and summer conditions in Table 5-4.

Table 5-4. 24-Hour sample concentration ranges (mg/m^3) of methanol in winter and summer in four Canadian cities for indoor and outdoor air[a]

Scenario	Indoor		Outdoor	
Season	**Geometric mean (arithmetic mean)**	**P5–P95**	**Geometric mean (arithmetic mean)**	**P5–P95**
Summer	0.196 (0.250)	0.035–0.518	0.018 (0.021)	0.008–0.034
Winter	0.150 (0.197)	0.056–0.433	0.017 (0.023)	0.003–0.085

[a] The highest means among the 4 cities and the 5th and 95th percentiles (P5 and P95) are given.

Methanol emissions from industrial production and use can lead to inhalation exposures for those residing in the vicinity of the industrial facilities. Methanol emission rates were determined using National Pollution Release Inventory (NPRI) data and correlated to the highest emissions and exposure potentials (NPRI 2014) for a methanol-producing facility that had the highest production volume and proximity to residential areas. This upper-bound emission scenario was used in SCREEN3 (1996) to determine the dispersion of methanol at various distances from the sources of industrial air release. SCREEN3 is a screening-level Gaussian air dispersion model based on the Industrial Source Complex (ISC) model for assessing pollutant concentrations from various sources in an industry complex. The driver for air dispersion in the SCREEN3 model is wind. A maximum exposure concentration is calculated using a built-in meteorological data matrix of different combinations of meteorological conditions, including wind speed, turbulence, and humidity. This model estimates concentrations of pollutants in air resulting from point, area, and volume source releases. SCREEN3 gives the maximum concentrations of a substance at chosen receptor heights and at various distances from the release source, in the direction downwind of the prevalent wind, 1 hour after a given release event. For point emission sources, the maximum 1-hour exposure estimate (as assessed by the ISC Version 3) is multiplied by a factor of 0.4 to account for variable wind direction to give an estimate of the air concentration over a 24-hour exposure (US EPA 1992). For exposures over the span of 1 year, it can be expected that with changing wind directions, the substance air concentrations within an area release source may not vary to the same extent as those of point release sources. The meteorological conditions giving rise to a maximum 1-hour exposure can persist for a longer duration. Thus, the maximum concentration for 1 year is determined by multiplying the maximum 1-hour concentration by a factor of 0.2. An exposure scenario was developed for residential homes in the vicinity of a 600 × 600 m^2 emission release area (industrial facility). Because of various activities in the industrial facility that caused local turbulence, the total facility area was considered to be the area emission source. A receptor height corresponding to the average height of Canadians (1.74 m) was used in the dispersion calculations. The parameters used to model the dispersion of the industrial facility releasing methanol are given in Table B-1 (Appendix B).

The variations in the concentration of methanol as a function of the distance from the centre of the industrial release site for a receptor height of 1.74 m are given in Table B-2 (Appendix B). The annualized ambient maximum methanol concentration is greatest at 800 m from the point of release and is estimated to be 0.53 mg/m^3 (see Table B-2 in Appendix B). This concentration is a worst-case estimate that does not account for the physical-chemical properties of methanol nor its degradation in air.

Methanol occurs naturally in humans, animals and plants. Normal diets and metabolism are a source of exposure and contribute to background methanol levels in blood. The general population may be exposed to methanol from the diet via consumption of fresh fruits, vegetables, fruit juices, foods containing the artificial sweetener aspartame, and fermented beverages such alcoholic drinks or kombucha tea (US EPA 2013). The average blood methanol level in a healthy American population was found to be 0.73

mg/L, with a range of 0.32 to 2.61 mg/L. The US EPA estimates that diet alone would not increase methanol blood levels above 2.5 mg/L (OECD 2004).

In Canada, methanol is a permitted food additive for use as a carrier solvent for meat and egg marking inks that are applied directly on the meat or the shell for branding or other designation. In this application, it must be used in accordance with Good Manufacturing Practice as per section B.01.045 of the *Food and Drug Regulations* (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, dated December 2016; unreferenced). All reasonable uses of these products involve thermal treatment of the meat or discarding of the shell.

There are other permitted uses of methanol as a food additive. It may be used as an extraction solvent in the manufacture of certain food ingredients (natural extractives, spice extracts, hop extract, and the sweetener steviol glycosides). In these instances, there are limits on the residual amount of methanol in food. The permitted food additive uses and maximum permissible residue levels are summarized in Table 5-5.

Table 5-5. Maximum residues of methanol permitted in food

Food additive use	Maximum permissible residue
Natural extractives; spice extracts	50 ppm
Hop extract[a]	2.2%
Steviol glycosides	200 ppm
Ethyl alcohol denatured with methanol is permitted in vegetable oil seed meals	10 ppm

[a] In accordance with subparagraph B.02.130(*b*)(v) and paragraph B.02.133(*a*) of the *Food and Drug Regulations*

Methanol also occurs naturally in fresh fruits and vegetables, and products made from them such as juices, sauces, alcoholic beverages, and vinegar. Food storage temperature and duration, as well as processing techniques such as pasteurization, can influence the concentration of methanol in processed foods (Hou et al. 2008; Shaw et al. 2000).

Alcoholic beverages are regulated as food and, as such, they are expected to comply with the general provisions under section 4(1)(a) of the F&DA, which stipulates that no person shall sell an article of food that has in it or on it any poisonous or harmful substance. There are no specific provisions within the *Food and Drug Regulations* governing methanol in alcoholic beverages or any other type of food. Health Canada has not developed maximum levels for methanol in alcoholic beverages, but has provided guidance to other federal departments and provincial liquor control boards on methanol concentrations in alcoholic beverages that are not expected to pose a concern to consumers. Provincial liquor control boards may establish limits for methanol in alcoholic beverages. For example, the Liquor Control Board of Ontario references regulations limiting methanol to 400 mg/L in different drinks (LCBO 2013).

Methanol can be produced within the human body by metabolic processes as well as during the digestion of certain food additives and ubiquitous plant compounds such as pectin (Dorokhov et al. 2015). The present assessment strictly quantified exposure to methanol that is present in food at the time it is consumed.

The occurrence data used to estimate dietary exposure to methanol were predominantly sourced from the Volatile Compounds in Food (VCF) database (Nijssen 1953–2017). For each food and beverage category in the database, the highest concentration of methanol reported was conservatively applied to represent the food category. In cases where methanol concentrations were of a similar magnitude between multiple related food categories, these foods were combined into a single category and the highest reported methanol concentration of all applicable foods was applied to the entire category (e.g., all non-citrus fruit). Where additional studies reported higher concentrations of methanol than the maximum from the VCF database, these higher concentrations were applied instead (Table C-1 of Appendix C).

The maximum methanol concentrations in foods and alcoholic beverages that were used in the present assessment ranged from 0.009 ppm in dairy products to 560 ppm in tomato juice, with the exception of pear brandy, which had higher reported methanol concentrations of up to 9300 ppm (Table C-1 of Appendix C).

The food consumption data used in the present assessment were from the Canadian Community Health Survey (CCHS) (Statistics Canada 2015). As brandy consumption was not captured in the CCHS survey, the 0.7% market share of all types of brandy in Canada (Nielsen 2017) was applied to the combined consumption of spirits reported in the CCHS survey (whiskey, vodka, rum and gin) to generate a consumption rate for brandy.

Health Canada's estimate of dietary exposure to methanol was derived by multiplying the maximum concentration of methanol assumed for each food item or category (Table C-1 of Appendix C) with the quantity of that food reportedly consumed by each respondent. This yielded a distribution of methanol exposure estimates for various age groups (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated February 9, 2018; unreferenced).

To estimate methanol exposure from its potential use as an extraction solvent, the maximum permitted residue levels indicated in Column 3 of the *List of Permitted Carrier or Extraction Solvents* were employed along with consumption information from the 2015 CCHS. However, dietary methanol exposure from its use as an extraction solvent in the manufacture of steviol glycosides was obtained from an assessment conducted by the Food Directorate in 2016, which employed 2004 CCHS (Statistics Canada 2004) consumption figures and assumed that steviol glycosides are used in all foods in which they are approved for use and contain methanol at the maximum permitted residue level. Dietary exposure to methanol from its potential use as a carrier solvent in meat and egg marking inks and as a component in food packaging materials was not

calculated as it is expected to be negligible in comparison to exposure from other food additive uses.

Dietary exposure to methanol from alcoholic beverages, natural sources (defined as all natural dietary sources other than alcoholic beverages) and potential food additive uses are presented in Table 5-6. As many foods containing methanol are a regular part of the diet of Canadians, 90th percentile exposure estimates were calculated. The 90th percentile is representative of 'all persons'.

Table 5-6. Estimated dietary exposure to methanol from alcoholic beverages, natural sources, and potential food additive uses[a]

Age group (males and females) (years)	Alcoholic beverages	Natural sources	Food additives
	Mean (P90)	Mean (P90)	Mean (P90)
1–3	N/A (N/A)	2.35 (5.70)	0.25 (0.56)
4–8	N/A (N/A)	2.13 (5.08)	0.25 (0.48)
9–13	N/A (N/A)	1.06 (2.49)	0.20 (0.40)
14–18	N/A (N/A)	0.74 (1.78)	0.11 (0.23)
19–30	0.10 (0.36)	0.64 (1.75)	0.06 (0.13)
31–50	0.13 (0.48)	0.59 (1.53)	0.16 (0.32)
51–70	0.20 (0.76)	0.49 (1.25)	0.09 (0.20)
71+	0.13 (0.51)	0.56 (1.35)	0.06 (0.13)

Abbreviation: N/A, not applicable

[a] The mean and 90th percentile (P90) values are given as mg/kg bw/day.

Alcoholic beverages and potential food additive uses make small contributions to dietary methanol exposure relative to natural dietary sources (Table 6-6). The food category contributing most significantly to natural dietary sources of methanol exposure was "tomatoes and tomato sauces," which represented 30% of the exposure in all age groups combined, as well as for children 1 to 3 years of age.

5.6.1.2 Exposure from products available to consumers

Dermal exposures

Methanol has a molar mass of 32.04 g/mol, a high vapour pressure (12 790 hPa at 20 °C) and a low octanol-water partition coefficient (between –0.82 and –0.64). As a result, methanol is expected to volatilize quickly when applied to the skin, and the primary route of exposure to dermally applied methanol is inhalation. This is supported by a study of dermal application of hand sanitizers containing ethanol that concluded that the primary route of exposure to ethanol from this product was inhalation (Ardnt et al. 2014). Methanol is lighter than ethanol (32.04 g/mol methanol vs. 46.07 g/mol for ethanol) and has a higher vapour pressure and a lower octanol-water partition coefficient. As such, it is expected to have an even shorter skin evaporation half-life than ethanol.

Methanol present in products intended for dermal application (in particular the topical cosmetic and natural health products in Table 6-3) is assumed to evaporate shortly after application. Therefore, the routes of human exposure to methanol are via inhalation and oral intake.

Inhalation exposure

The level of methanol in indoor air in Canadian homes can be attributed to various sources, including cosmetics intended for dermal use, household cleaning products, home maintenance products, and other aerosol products. For the purpose of assessing risk from potential long-term exposure to methanol in the home, the geometric mean and highest 95th percentile value of methanol for Canadian non-smoking homes were selected from air sampling studies conducted in homes located in four Canadian cities, as given in Table 6-4. The levels—0.20 and 0.5182 mg/m^3, respectively—are considered to represent typical estimates of indoor air levels of methanol.

The product available to consumers with methanol with repeat daily household use and highest expected exposure is an all-purpose spray cleaner containing 5 w/w% methanol. Using the ConsExpo Web exposure factors for all-purpose spray cleaner given in Table B-4 of Appendix B, a mean concentration on the day of exposure of 0.62 mg/m^3 is calculated.

To estimate short-term inhalation exposure to methanol from the use of cosmetics and/or NHPs, scenarios were selected that represent an upper-bound exposure. A hairstyling product was selected on the basis of largest amount used and highest percent of methanol present in the product (3%). It is considered that the methanol in this product evaporates quickly and that inhalation exposure becomes the exposure route for methanol from the use of this product. The exposure factors for the use of hairstyling products are given Table B-4 (Appendix B). The resulting mean inhalation event concentration was determined to be 5.1 mg/m^3 using ConsExpo (RIVM 2006, Ficheux et al. 2016). Amortizing this 10-minute exposure over 1 day gives an average concentration of 0.35 mg/m^3. A muscle rub product with a sponge applicator with 50% methanol is also considered. Based on the use of 2 mL of product with each application, the quick evaporation of methanol in this product upon contact with skin, and the exposure factors given in Table B-4 (Appendix B), the mean inhalation concentration on the day of use is 2.0 mg/m^3. A short-term inhalation exposure to methanol from paint and varnish remover use with 5% to 35% methanol content was considered. The ConsExpo Exposure to Vapour model with the evaporation mode was used (RIVM 2018). Exposure factors for the calculation of the inhalation exposure to methanol from this scenario are given in Table B-3 (Appendix B) for a range of project sizes (related to amount of product used and release areas) and room ventilation rates. In the paint and varnish remover products, methanol acts as a cosolvent and is essential to the proper action of the paint remover (Wollbrinck 1993). As a result, to prevent the loss of this solvent, paint remover products are often in gel form (MSDS 2013a,c, 2015h,j, 2018a; TDS 2019) and, as such, act as an evaporation barrier for methanol (Wollbrinck 1993).

To consider the presence of this evaporation barrier, an emission factor of 50% was considered for the release of methanol from the paint remover.

For small projects, a mean methanol concentration on the day of exposure (amortized over 24 hours) was 5.0 to 10.5 mg/m^3 for products with 5% methanol and 37 to 72 mg/m^3 for products with 35% methanol. For larger projects, the mean methanol concentration on the day of exposure for the range of products was between 46 mg/m^3 and 610 mg/m^3.

Products used to remove paint for bathtub resurfacing may also have methanol contents between 5% and 35%. Exposure factors for the calculation of the inhalation exposure to methanol from this scenario are given in Table B-3 (Appendix B). The mean concentration of methanol on the day of exposure for bathtub resurfacing in a bathroom was 65 mg/m^3 and 460 mg/m^3 for 5% and 35% methanol containing products, respectively.

The mean event and peak concentrations determined for each of these scenarios are given in Table B-3 (Appendix B).

5.6.2 Health effects assessment

Methanol was reviewed internationally by ECHA (2015, 2016a) and the US EPA (2013a,b). These reviews were used to inform the health effects assessment of this substance. A literature search was conducted up to the period of April 2020, and no studies that could result in a different health effects assessment from that of these agencies was identified.

The US EPA (2013a) evaluated various methanol toxicity studies comprising data from different species and endpoints and derived a reference dose (RfD) of 2 mg/kg bw/day and a reference concentration (RfC) of 20 mg/m^3 based on developmental effects. The RfD and RfC values were calculated for a population with a background blood methanol level at or below 2.5 mg/L as a result of metabolism and consumption of foods (fruits and vegetables) with naturally occurring methanol. Developmental effects included skeletal (cervical rib or supernumerary rib) malformation, cleft palate, and exencephaly in mice pups in the absence of any maternal toxicity, reduced brain weight in adult and developing rat pups, and indications of developmental effects in monkeys following repeated-dose inhalation exposure (Kavet and Nauss 1990; Burbacher et al. 1999a, 1999b, 2004a, 2004b; Rogers et al. 1993; NEDO 1987; Fisher et al. 2000, OECD 2004c). The US EPA indicated that these studies showed consistent developmental effects at similar doses in mice and rats. Notably, the biological significance of these effects is considered relevant to humans as increases in supernumerary ribs and decreases in brain weight may occur in humans and are considered adverse effects (US EPA 2013a, 2013b; Chernoff 2004). Due to the developmental nature of the effects, this RfD is considered relevant to both short- and long-duration exposures. The US EPA noted that although there are uncertainties regarding the relevance to humans of the effects seen in rodents, there was sufficient evidence of potential developmental effects

in primates, as well as a lack of knowledge about the metabolism of methanol in human infants, to justify the use of the rodent studies to determine inhalation and oral points of departure.

The ECHA Committee for Risk Assessment (RAC) determined that based on available information, there was insufficient evidence for classifying methanol for developmental toxicity in humans (ECHA 2015d). They concluded that the most relevant endpoint for general population exposure via the inhalation and dermal routes was transient neurological effects and supported derived no-effect levels (DNEL) of 43.3 mg/m^3 and 6.66 mg/kg bw/day for these routes of exposure based on existing European Union (EU) indicative occupational exposure limit values. ECHA subsequently proposed an oral DNEL of 88 mg/kg bw to be protective of acute methanol toxicity by ingestion. This DNEL was based on significantly reduced visual acuity at 260 mg/kg bw (ECHA 2016b).

Short-duration exposures to airborne methanol in humans has been reported to cause dizziness, headache, nausea, insomnia, blurred vision and conjunctivitis (US EPA 2005b). In a workplace study, exposure to mean air concentration of 1060 ppm (1400 mg/m^3) of methanol was reported to cause significantly higher frequencies of headaches, nausea, dizziness and blurred vision in school teachers (Frederick et al. 1984). In another study, workers reported eye irritation following 25-minute exposure to 1025 ppm (1300 mg/m^3) of airborne methanol (NIOSH 1981).

The genotoxic potential of methanol has been reported to be negative in the majority of *in vitro* and *in vivo* assays (IPCS 1997b, 2001; NTP 2004; OECD 2004c,d). Methanol has not been classified as a carcinogen by the US EPA, IARC or NTP (Cruzan 2009; IARC 2018).

5.6.3 Characterization of risk to human health

Inhalation exposure

The RfC for inhalation of methanol of 20 mg/m^3 derived by the US EPA was compared to measured and estimated exposures of Canadians to methanol.

The highest 95th percentile outdoor concentration for methanol reported in Table 6-4 was 0.085 mg/m^3. The maximum methanol concentration for individuals living within 1000 m of a methanol industrial facility was estimated to be 0.52 mg/m^3. Both of these outdoor methanol concentrations are lower than the RfC and therefore not of concern.

The highest 95th percentile indoor concentration of methanol determined by indoor air monitoring in Canadian cities is 0.52 mg/m^3 (Table 6-4). The 24-hour air concentration resulting from the use of an all-purpose spray cleaner with 5% w/w methanol was estimated to be 0.62 mg/m^3. For inhalation exposure to methanol from the use of a hairstyling product and muscle pain relief liquids, the concentrations on day of exposure is 0.35 and 2.0 mg/m^3. Other cosmetic products (including skin moisturizer) and NHPs lead to lower exposures. All of these indoor methanol concentrations are lower than the RfC and therefore not of concern.

For the inhalation exposure to methanol from the use of paint and varnish remover, the range of air concentrations on the day of exposure (amortized over 24 hours) for small and large projects is determined to be 10.5 mg/m^{3}to 611 mg/m^3. The smaller projects (as specified in Table B-3 of Appendix B as using 1000 g or less of product) using paint removers with 5% methanol gave average 24-hour concentrations of methanol of 5.0 mg/m^3 to 10.5 mg/m^3, which are not considered to be of concern when compared to the RfC of 20 mg/m^3. The 24-hour average concentrations of methanol from use of paint remover in small projects with 35% methanol were 37 mg/m^3 to 72 mg/m^3. These concentrations are of concern when compared to the RfC of 20 mg/m^3.

The 24-hour average concentrations of methanol from use of paint remover in larger projects (using more than 1000 g of product) with 5% to 35% methanol were 46 mg/m^3 to 610 mg/m^3. These concentrations are of concern when compared to the RfC of 20 mg/m^3.

The 24-hour average concentrations of methanol from use of paint remover in bathtub resurfacing with 5% and 35% methanol were 65 mg/m^3 and 460 mg/m^3, respectively. These concentrations are of concern when compared to the RfC of 20 mg/m^3.

For large projects and bathtub resurfacing, the exposures are also of concern when compared to the methanol DNEL of 43 mg/m^3 proposed by ECHA. Small projects with products containing 35% w/w methanol can also lead to exposures of concern when compared to the methanol DNEL of 43 mg/m^3.

It is noted that concentrations higher than 1025 ppm (1300 mg/m^3) for airborne exposure to methanol were observed to lead to irritation and dizziness following short-duration exposures in workers (US EPA 2005b; Frederick et al. 1984; NIOSH 1980). Inhalation exposures for paint or varnish remover scenarios, which lead to mean event or peak concentrations of methanol higher than this value, may be self-limited by the discomfort that the user may feel while exposed to the product.

The use of methanol-containing paint and varnish remover products encompassed in this inhalation exposure assessment are identified as a concern for human health as their use can lead to inhalation exposures above the RfC levels. All other calculated inhalation exposures are at or below the RfC levels and therefore do not pose a concern to human health.

Oral exposure

In establishing their RfD, the US EPA (2013a) assumed a maximum natural background dietary exposure rate of approximately 14.3 mg/kg bw/day. Exposure from foods with naturally occurring methanol levels (Table 6.6) is not expected to constitute a risk to the public.

With respect to food additive uses, the use of methanol as a solvent in ink is not expected to permeate egg shells or persist in meat after it is cooked. These applications are therefore not expected to be a source of methanol exposure to the general

population. Further, based on volatility, any residual methanol solvent is also unlikely to remain in foods that are permitted to contain methanol as a food additive (such as those listed in Table 6-3) after they are exposed to air. Vegetable oils, spices, and sweeteners, used in the preparation of foods and beverages, are likely to further release residual methanol if they are heated during preparation or before consumption of foods. The use of hop extract is limited, and the general population is not anticipated to consume this product in its pure form.

Based on consumption amounts and the use patterns of food products for which the use of methanol as a solvent is permitted, exposure exceeding the 2 mg/kg bw/day RfD is not expected.

The estimated dietary exposures to methanol from alcoholic beverages and from its potential use as a food additive (excluding natural sources) as identified in Table 6-6 are below the RfD of 2 mg/kg bw/day for all age groups, including the 90th percentile of users.

Small amounts of methanol may be present as a solvent in certain NHPs that are in tablet form. However, exposure from this source is not expected to exceed 2 mg/kg bw/day and is not of concern.

Dermal exposure
Due to the rapid evaporation of methanol applied to the skin, exposures via the dermal route are not expected.

5.7 Uncertainties in evaluation of risk to human health

For the estimation of oral exposures, the maximum methanol concentrations were applied for all foods or food categories. This is a conservative assumption. In cases where data on the concentrations of methanol in food were only available for specific items within a given food category, the maximum methanol concentration in a given food item was assumed to be representative of the broader category as a whole. The effect of this assumption on the estimated methanol level will depend on the specific food category and representative food chosen. For the use of methanol as an extraction solvent, it was assumed that all foods in which methanol is permitted contained methanol at the maximum permitted residue level. This is a conservative assumption. It was assumed that all foods permitted to contain steviol glycosides are sweetened using this particular sweetener at the maximum permitted level, which is also a conservative assumption.

6. 1-Butanol

6.1 Substance identity

Information regarding the identity of 1-butanol is summarized in Table 6-1 (PubChem2004-).

Table 6-1. Substance identity of 1-butanol

CAS RN	DSL name	Molecular formula	Molecular structure	Molecular weight (g/mol)
71-36-3	1-Butanol	$C_4H_{10}O$		74.12

6.2 Physical and chemical properties

Measured physical and chemical properties of 1-butanol are given in Table 6-2 (ChemIDplus 2017). Additional physical and chemical properties data are presented in ECCC (2016b).

Table 6-2. Measured physical and chemical properties of 1-butanol

Melting point (°C)	Boiling point (°C)	log K_{ow} (dimensionless)	Water solubility (mg/L)	Vapour pressure (mm Hg)
–89.8	117.7	0.88	8.50×10^4	6.7

1-Butanol is expected to volatilize from water surfaces. Estimated volatilization half-lives for a model river and model lake are 3.7 days and 29 days, respectively.

6.3 Sources and uses

1-Butanol occurs in nature as a result of fermentation processes. It is also manufactured through a variety of synthetic routes. According to information from a survey issued pursuant to section 71 of CEPA, 1-butanol was not reported to be manufactured in Canada in 2011, but 68 000 kg of 1-butanol were reported to be imported into Canada that year (Environment Canada 2013).[6]

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, 1-butanol is present in cosmetic products in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 19, 2016; unreferenced). The nature of the products and highest concentration of 1-butanol is given in Table 6-3. The concentrations show the amount of 1-butanol in the formulated products and do not take into account any dilution prior to or during use. 1-Butanol is not on the Cosmetic Ingredient Hotlist.

[6] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

Table 6-3. Cosmetic products containing 1-butanol

Number of products	Products and maximum concentration
46	Skin products 0.1% Nail products 10%

1-Butanol may be used as a component in food packaging materials (epoxy, polyethylene- or polyurethane-based materials, coatings, polyvinyl chloride, polyester, printing inks, adhesives) with no direct food contact. Therefore, exposure of the general population is not expected. The substance is known to be used as a food flavouring agent in the United States and the EU, and it is therefore possible that the substance is present as a food flavouring agent in foods sold in Canada (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2016; unreferenced).

1-Butanol is also used as a non-medicinal ingredient in a number of oral and dermally applied NHPs, as well as non-prescription and prescription drugs, including products formulated as tablets, capsules, and creams (personal communication, email from the Natural and Non-prescription Health Products Directorate and Therapeutic Products Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 26 and November 1, 2016; unreferenced).

In pesticides, 1-butanol is used as a formulant (PMRA 2010).

1-Butanol is also present in a range of products available to consumers. The product categories and concentration ranges are shown in Table 6-4.

Table 6-4. Products available to consumers in Canada containing 1-butanol

Product category	Product type / maximum 1-butanol weight %	Reference
Automotive care	Wax (3%–7%) Fuel injector cleaners (20%–30%)	MSDS 2014a MSDS 2014b
Solvent	Solvent in spray paints (5%) Epoxy adhesives (5%) Wood gloss paint / lacquer (5%–20%) Solvent for markers (6%)	MSDS 2014c MSDS 2015b MSDS 2015c MSDS 2016a

6.4 Environmental fate and behaviour

6.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), 1-butanol is not expected to persist in air, water, sediment, or soil (ECCC 2016b).

6.4.2 Potential for bioaccumulation

Due to a low log K_{ow} and low bioconcentration factor (ECCC 2016b), 1-butanol is not expected to bioaccumulate in organisms.

6.5 Potential to cause ecological harm

6.5.1 Characterization of ecological risk

The ecological risk of 1-butanol has been characterized using the ecological risk classification of organic substances (ERC) approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for 1-butanol, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

On the basis of low hazard and low exposure classifications according to information considered under ERC, 1-butanol is classified as having a low potential for ecological risk. It is therefore unlikely that this substance is resulting in concerns for the environment in Canada.

6.6 Potential to cause harm to human health

6.6.1 Exposure assessment

6.6.1.1 Environmental media and food

There is a potential for 1-butanol to be present in water and air in limited quantities. Based on calculated results from a level III fugacity model, 1-butanol is expected to partition primarily to the air (83.5%) with the remainder to soil (5.9%) and water (10.6%) (OECD 2001a). It has been shown to biodegrade rapidly in aerobic, aqueous biodegradation tests and therefore is not expected to persist in aquatic environments. It is also not expected to remain in surface soils due to rapid evaporation to the air.

To assess potential typical exposures for the general population to 1-butanol in ambient air, Bari et al. (2015) conducted air monitoring studies inside and outside residences. Indoor and outdoor air monitoring studies were performed in Edmonton (Health Canada 2013), Halifax (Health Canada 2012), Regina (Health Canada 2010a), and Windsor (Health Canada 2010b). These studies report on seasonal variations in 1-butanol, in both residential indoor and outdoor environments. The geometric mean, arithmetic mean, 5th percentile (P5), and 95th percentile (P95) concentrations from sampling over 24-hour periods are given for winter and summer conditions in Table 6-5.

Table 6-5. Summer and winter indoor and outdoor air concentrations [µg/m^3] of 1-butanol[a]

Scenario	Indoor		Outdoor	
Season	Geometric mean (arithmetic mean)	P5–P95	Geometric mean (arithmetic mean)	P5–P95
Summer	5.016 (8.880)	1.240–19.59	0.474 (0.577)	0.228–1.158
Winter	1.464 (2.581)	0.408–8.500	0.085 (0.120)	0.042–0.284

[a] The highest mean and extremes of the minimum and maximum range among the four cities are given along with the 5th to 95th percentile [P5-P95] range [µg/m^3]).

This indoor concentration reflects daily exposure to 1-butanol from multiple sources.

Based on a comparison of production volumes, exposure to 1-butanol from foods that naturally contain this substance is expected to be greater than exposure from its use as a food flavouring agent (Stofberg and Grundschober 1987). Internationally, JECFA evaluated 1-butanol as a food flavouring agent and estimated the corresponding per capita intake of 1-butanol at 8100 µg/day (140 µg/ kg bw/day) for the US population (International Organization of the Flavor Industry 1995; National Academy of Science 1987, both cited in WHO JECFA 1999). JECFA concluded there was “no safety concern at estimated levels of intake” for 1-butanol when used as a food flavouring agent. In the absence of Canadian data, the JECFA per capita intake estimate for the US population is an acceptable estimate of possible Canadian dietary exposure for the general population 1 year of age and older from its potential use as a food flavouring agent (personal communication, email from Food Directorate, Health Canada to Existing Substances Risk Assessment Bureau, Health Canada, 2018; unreferenced).

6.6.1.2 Exposure from products available to consumers

As shown in Tables 7-3 and 7-4, 1-butanol is present in products available to consumers, including cosmetics and home and automotive care products. 1-Butanol is also used as a non-medicinal ingredient in a number of NHPs, as well as prescription and non-prescription drugs. The products with highest potential exposure to 1-butanol are considered in the scenarios below for each product type.

Inhalation exposure

Long-term inhalation exposure concentrations to 1-butanol have been determined in Bari et al. (2015) and are reported in Table 7-5.

A number of sentinel products were chosen to assess the short-term inhalation exposures to 1-butanol. A short-term inhalation exposure to 1-butanol from spray paint use with 5% w/w 1-butanol content is considered. The exposure factors for the use of the spray paint are given in Table B-5 (Appendix B). This scenario gave a mean 1-butanol concentration on the day of exposure of 1.0 mg/m^3 and an external dose of 0.23 mg/kg bw on the day of exposure.

There are two groups of epoxy products containing 1-butanol. One group consists of a two-part acrylic coating which is used to resurface bathtubs (MSDS 2015b). The exposure factors for the use of the acrylic coating are given Table B-6 (Appendix B). Using 900 g of the products and the exposure assumptions listed in Table B-6 (Appendix B) resulted in a mean 1-butanol concentration on the day of exposure of

0.72 mg/m^3. Using a breathing rate of 16.3 m^3/day and an average adult weight of 70.9 kg gives an exposure dose of 0.17 mg/kg bw/day. Given that package directions include ensuring increased ventilation during application of the products, the ventilation factor and therefore the exposure are highly conservative.

A short-term inhalation exposure to 1-butanol from lacquer/varnish use with 5% to 20% 1-butanol content is considered (MSDS 2015c, 2016a). Using the exposure factors given provided in Table B-7 (Appendix B) gives a mean 1-butanol concentration range on the day of exposure of 3.3 to 13.2 mg/m^3. Using a breathing rate of 16.3 m^3/day and an average adult weight of 70.9 kg gives an exposure dose range of 0.8 mg/kg bw/day - 2.4 mg/kg bw/day.

Oral exposure

To estimate the daily exposure to 1-butanol present as a non-medicinal ingredient in NHPs as well as in prescription and non-prescription drugs formulated as capsules or tablets, the maximum potency per unit dose of 0.02 mg outlined for tablet, extended release in the US FDA's Inactive Ingredient Search for Approved Drug Products was used (US FDA 2019). Assuming for the purpose of this scenario a daily dose of four extended release tablets translates to daily oral exposures of 4 × 0.02 / 59.5 = 0.0013 mg/kg bw/day for teenagers and 4 × 0.02 / 70.9 = 0.0011 mg/kg bw/day for adults.

Dermal exposure

In vitro experiments on human skin samples exposed to neat 1-butanol in unventilated and ventilated conditions resulted in absorptions of 2.2% to 9.4% and <1%, respectively (Boman and Maibach 2000). 1-Butanol is volatile and allowing evaporation from the skin leads to low total absorption values.

The scenario that results in the highest exposure for cosmetic products is nail polish with 1-butanol at concentrations of up to 10% by weight. For adults, using the default value of 0.16 g for application of nail polish with instant application and a conservative value of 10% dermal absorption gives systemic exposure on the day application of 0.022 mg/kg bw for adults weighing 70.9 kg. For teenagers, using the default value of 0.16 g for application of nail polish with instant application and a conservative value of 10% dermal absorption gives systemic exposure on the day of application of 0.027 mg/kg bw for teenagers weighing 59.4 kg. These values are considered conservative as they do not consider evaporation of 1-butanol.

Dermal exposure to 1-butanol from a body moisturizer categorized as an NHP with a concentration of 0.1%, using the default values of 8.6 g and 10 g for teenagers and adults, respectively, was estimated. A frequency of application of 1.1 times/day and a conservative value of 10% dermal absorption provides exposure doses of 0.016 mg/kg bw/day and 0.015 mg/kg bw/day for teenagers and adults weighing 59.4 kg and 70.9 kg, respectively.

6.6.2 Health effects assessment

1-Butanol has been reviewed internationally and that review have been used to inform the health effects characterization in this assessment (US EPA 2011; OECD 2001a).

The US EPA (2011) derived an RfD of 0.09 mg/kg bw/day for 1-butanol based on the most sensitive neurodevelopmental effects (dilation of lateral or third ventricles) of the brain and skeletal effects (delayed ossification of sternum) in rat fetuses, born to Wistar (Imp: DAK) dams exposed to 300, 1000, or 5000 mg/kg bw/day of 1-butanol for 8 weeks before mating, during mating (3 weeks) and until GD 20. Fetuses born to dams in the highest dose group were also significantly smaller in size as compared to controls. However, no mortality or adverse effects were reported in any dams treated with 1-butanol (Sitarek et al. 1994). Fetal skeletal malformations were also reported in reproductive or developmental studies following inhalation exposure to a dose range of 18 000 mg/m^3 to 24 000 mg/m^3 of 1-butanol, 7 hours/day on GD 1 to 19 in Sprague-Dawley rats (Nelson et al. 1989a, b). However, rats were exposed to very high doses of 1-butanol in these studies (US EPA 2011).

Notably, subchronic (90-day) inhalation exposure to 154 or 308 mg/m^3 of 1-butanol vapours (6 hours/day, 5 days/week) caused a progressive increase in poor motor coordination (neuromuscular effects) in adult male Wistar (Imp: DAK) rats. A significant decrease was also seen in hemoglobin concentration in both dose groups, while a decrease in red blood cells and an increase in white blood cells were observed only in the highest dose group. However, no signs of toxicity were observed in rats in any treatment group. The authors identified a NOAEL of 154 and a lowest-observed-adverse-effect level (LOAEL) of 308 mg/m^3 in this study (US EPA 2011; Korsak et al.1994).

An ECHA (2018) evaluation report concluded that 1-butanol is not a concern in terms of reproductive or developmental toxicity based on lack of developmental effects in rat fetuses born to Sprague-Dawley dams given 316, 1,454 or 5,654 mg/kg bw/day of 1-butanol via drinking water throughout pregnancy (GD 0 to 20) (Ema et al. 2005). The study authors identified a NOAEL of 1454 mg/kg bw/day for both dams and fetuses. However, the US EPA estimated a developmental LOAEL of 5654 mg/kg bw/day for developmental effects (decrease in fetal body weight, increased incidence of skeletal variations) and a NOAEL of 1454 mg/kg bw/day from this study (US EPA 2011).

In the present assessment, the neurodevelopmental effects reported in Sitarek et al. (1994) were considered to have occurred in a suitable rat model (Noritake et al. 2013; Zmyslony et al. 2004; Jedrychowski et al. 1990) and deemed biologically relevant to developing human infants (Cherian et al. 2003). Additionally, Sitarek et al. (1994) was used by the US EPA for derivation of RfD as it was considered a well-designed study that examined the critical effects of 1-butanol in the developing brain.

6.6.3 Characterization of risk to human health

As developmental effects were observed in the absence of maternal toxicity, subpopulations of reproductive age (teens and adults) were the focus of the risk characterization for all but long-duration inhalation exposures.

Inhalation exposure

The 95th percentile of the long-term indoor inhalation exposure to 1-butanol from air monitoring measurements in Canada was 0.02 mg/m^3. When the lowest-observed-adverse-effect concentration (LOAEC) of 308 mg/m^3 was adjusted to 24 hours/day and 7 days/week exposures to give a LOAEC of 55 mg/m^3 for neurobehavioural deficit, a margin of exposure (MOE) of 2800 was obtained. This MOE is considered both adequate to address the uncertainties in the exposure and health effects databases and protective of exposures via environmental media.

A short-term inhalation scenario from the use of epoxy bathtub coating containing 5% w/w of 1-butanol gave a mean 1-butanol concentration on the day of exposure of 0.72 mg/m^3 and an exposure dose of 0.17 mg/kg bw/day. With the LOAEL of 300 mg/kg bw/day for developmental effects, this gives an MOE of 1800. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

A short-term inhalation scenario from the use of lacquer containing 5% w/w to 20% w/w of 1-butanol gave a mean 1-butanol concentration range on the day of exposure of 3.3 to 13.2 mg/m^3 or a dose range of 0.8 to 2.4 mg/kg bw/day. With the LOAEL of 300 mg/kg bw/day for developmental effects, this gives an MOE of 375 to 94. These MOEs are potentially inadequate to account for uncertainties in the health effects and exposure databases.

Oral exposure

Based on estimated exposures of 0.0013 mg/kg bw/day and 0.0011 mg/kg bw/day calculated from the scenario of four 0.02 mg 1-butanol-containing extended-release tablets per day and a LOAEL of 300 mg/kg bw/day for developmental effects, MOEs of 230 000 and 270 000 were obtained for teenagers and adults, respectively. These MOEs are considered adequate to address uncertainties in the exposure and health effects databases.

Based on an estimated dietary exposure of 0.140 mg/kg bw/day from the use of 1-butanol as a food flavouring agent and a LOAEL of 300 mg/kg bw/day for developmental effects, an MOE of 2100 was calculated for the general population 1 year of age and older. This MOE is considered adequate to address uncertainties in the exposure and health effects databases.

Dermal exposure

Based on a maximum systemic exposure of 0.027 mg/kg bw/day from nail polish with 10% 1-butanol, using a conservative value of 10% dermal absorption (Boman and Maibach 2000) and a LOAEL of 300 mg/kg bw/day for developmental effects, an MOE of 11 000 was obtained. This MOE is considered adequate to address uncertainties in the exposure and health effects databases.

Based on a maximum exposure of 0.016 mg/kg bw/day from moisturizer creams in the category of non-prescription drugs with 0.1% 1-butanol, using 10% dermal absorption (Boman and Maibach 2000) and a LOAEL of 300 mg/kg bw/day for developmental effects, an MOE of 18 000 was obtained. This MOE is considered adequate to address uncertainties in the exposure and health effects databases.

6.7 Uncertainties in evaluation of risk to human health

The dermal absorption of 10% used for 1-butanol is conservative, as this value is for neat 1-butanol applied to skin under unventilated conditions. There may be uncertainty in the oral to dermal and oral to inhalation route extrapolation for the endpoints used for the different exposure scenarios.

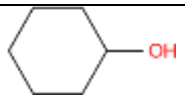
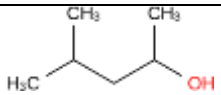
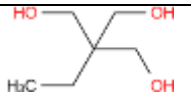
There can be uncertainty with regard to the exposure factors used in the scenarios for determining the inhalation exposure to 1-butanol. In particular, based on the nature of the products, the details of the use may differ from that characterized in the exposure scenario.

7. C6 Alcohols

7.1 Substance identity

Information regarding the identity of the C6 alcohols discussed in this assessment is summarized in Table 7-1 (PubChem2004-).

Table 7-1. Substance identity of C6 alcohols

CAS RN	DSL name (common name)	Molecular formula	Chemical structure	Molecular weight (g/mol)
108-93-0	Cyclohexanol	$C_6H_{12}O$		100.161
108-11-2	2-Pentanol, 4-methyl- (methyl isobutyl carbinol, MIBC)	$C_6H_{14}O$		102.177
77-99-6	1,3-Propanediol, 2-ethyl-2-(hydroxymethyl)- (trimethylolpropane, TMP)	$C_6H_{14}O_3$		134.175

7.2 Physical and chemical properties

Measured data for the physical and chemical properties of the C6 alcohols is given in Table 7-2 (ChemIDPlus 2017). Additional physical and chemical properties are presented in ECCC (2016b).

Table 7-2. Measured physical and chemical properties of C6 alcohols

Property	Cyclohexanol	MIBC	TMP
Melting point (°C)	25.4	‑90	58
Boiling point (°C)	160.8	131.6	289
log K_{ow} (dimensionless)	1.23	1.43	‑1.48
Water solubility (mg/L)	4.2×10^{-6}	1.64×10^{4}	1×10^{6}
Vapour pressure (mm Hg)	0.8	5.3	4.49×10^{-5}
Henry's law constant (atm-m^3/mol)	4.4×10^{-6}	4.45×10^{-5}	7.93×10^{-12}
Half-life in air (hours)	7.3	10.0	9.3

Cyclohexanol and MIBC are secondary alcohols and TMP is a primary alcohol, all composed of six carbons. Because of the differences in their molecular structures, these substances exhibit variation in physical and chemical properties.

The C6 alcohols are relatively volatile, have very high water solubility, high boiling points, and (with the exception of TMP) high vapour pressure. TMP has low vapour pressure due to stronger hydrogen bonding in this substance. In air, they react with photochemically-produced hydroxyl radicals, and the resulting half-lives are noted in Table 8-2. Cyclohexanol and MIBC are not susceptible to direct photolysis by sunlight (PubChem 2004-). MIBC is a moderately reactive ozone-forming substance, but cyclohexanol and TMP are not expected to be reactive in this regard. In soil, cyclohexanol and MIBC are expected to have high to very high mobility, and volatilization from moist soil surfaces is expected from both substances. In addition, MIBC may be biodegradable in soil. Neither is expected to absorb to suspended soils or sediment in water. TMP is not expected to have high mobility in soil due to its low soil (organic carbon–water) partition coefficient (K_{oc}) of 1. Likewise, it is not expected to volatilize from water surfaces due to its low Henry's law constant value, whereas cyclohexanol and MIBC are expected to volatilize from water surfaces.

7.3 Sources and uses

All the C6 alcohols evaluated in this assessment are high production volume chemicals. In industry, they are used as solvents and in polymer production, mining, and resin production. Commercially, they are present as ingredients in construction products, paints, and automotive care products. MIBC may be formed naturally in volatiles from mountain Beaufort cheese (concentration unknown) (Dumont and Adda 1978). MIBC is not found in other natural sources in significant amounts.

These alcohols are manufactured through a variety of synthetic routes. Total manufacturing and import volumes in Canada in 2011 as reported in response to a CEPA section 71 survey are shown in Table 7-3 (Environment Canada 2012).

Table 7-3. Summary of information on Canadian manufacturing and imports of the C6 alcohols subgroup submitted in response to a CEPA section 71 survey

Alcohol	Total manufacture (kg)[a]	Total imports (kg)[a]
Cyclohexanol	NR	770
MIBC	NR	1 500 000
TMP	NR	210 000

Abbreviations: NR, not reported above the DSL IU reporting threshold of 100 kg.
[a] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

These C6 alcohols have various industrial uses. Cyclohexanol is an important feedstock in the polymer industry, MIBC is used as a frother in mineral flotation and as a solvent in dyestuffs, oils, gums, resins, and waxes, and TMP is mainly consumed as a precursor to alkyd resins. All three substances are used as solvents. They are also present in a range of products available to consumers. The product categories and concentration ranges are shown in Table 7-4. The ranges shown indicate concentrations of the C6 alcohols in the formulated products and do not take into account any dilution prior to or during use.

Table 7-4. Products available to consumers sold in Canada that contain cyclohexanol, MIBC, and TMP and the percent alcohol in the product when available

Alcohol	Product category	Product type	Weight % in product
Cyclohexanol	Construction or paint	Ceramic glaze Hobby craft paint	25–50 2.5–10
	Automotive care	Internal combustion chamber cleaner [a] Engine tune-up [a]	5–15 5–10
MIBC	Construction or paint	Paint [a] Epoxy activator Lacquer [a] Specialty paint	7–18 7–13 5
	Automotive care	Lubricants [a] Engine treatment [a] Combustion chamber cleaner	 5–10 3–10
	Construction or paint	Floor covering [a]	
TMP	Other	Adhesive/sealants [a]	

[a] Non-confidential uses reported in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

As shown in Table 7-4, cyclohexanol, MIBC, and TMP are found in products available to consumers. They are mostly found in automotive care products and construction/paint products, though TMP is found in a limited number of cosmetic products as well.

The C6 alcohols may be used as components in the manufacture of food packaging materials and as incidental additives used in food processing establishments in Canada (see Table 7-5). Due to the high water solubility of TMP, it is not expected to be present in an unpolymerized form in these food packaging materials. Both cyclohexanol and MIBC are known to be used internationally as food flavouring agents, and it is therefore possible that the substance is present as flavouring agent in foods sold in Canada (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated December 2016; unreferenced).

Table 7-5. Possible uses for cyclohexanol, MIBC, and TMP in foods in Canada[a]

Alcohol	Food packaging materials	Incidental additives[b]	Food additive	Food flavouring agents	Potential for exposure
Cyclohexanol	Yes – components of inks, overlacquer, laminated film	Yes – boiler water additive	No	Yes	Yes
MIBC	Yes – component of films (not food contact layer)	No	No	Yes	Yes
TMP	Yes – component in adhesives, processing aid for film, pigments, can coating (including infant formula), side seams (including infant formula)	Yes – lubricant	No	No	Yes

[a] Personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated December 2016; unreferenced.
[b] While not defined under the *Food and Drugs Act* (FDA), incidental additives may be regarded, for administrative purposes, as those substances which are used in food processing plants and which may potentially become adventitious residues in foods.

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, of the C6 alcohols, only TMP is present in two cosmetic products in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 19, 2016; unreferenced). The nature of the products and highest concentration

of TMP are given in Table 7-6. The concentrations show the amount of TMP in the formulated products and do not take into account any dilution prior to or during use. None of these C6 alcohols are on the Cosmetic Ingredient Hotlist.

Table 7-6. Cosmetics in Canada containing TMP

Alcohol	In Cosmetics	Products and Concentration Range
TMP	2 products	Nail adhesive 3–10% Makeup/lip 3–10%

Only TMP is found in pest control products (PMRA 2010), as a formulant.

7.4 Environmental fate and behaviour

7.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), MIBC is expected to persist in air, but is not expected to persist in water, soil, or sediment. TMP is expected to persist in water, soil, and sediment, but is not expected to persist in air. Cyclohexanol is not expected to persist in air, water, sediment, or soil.

7.4.2 Potential for bioaccumulation

Given their low log K_{ow} values and low bioconcentration factors (ECCC 2016b), the three C6 alcohols are not expected to significantly bioaccumulate in organisms.

7.5 Potential to cause ecological harm

7.5.1 Characterization of ecological risk

The ecological risks of C6 alcohols have been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profiles for the C6 alcohols, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

The hazard and exposure classifications for the C6 alcohols are summarized in Table 7-7.

Table 7-7. Ecological risk classification results for the C6 alcohols

Substance	ERC hazard classification	ERC exposure classification	ERC risk classification
Cyclohexanol	low	low	low
MIBC	low	low	low

TMP	low	low	low

On the basis of low hazard and low exposure classifications according to information considered under ERC, cyclohexanol, MIBC, and TMP were classified as having low potential for ecological risk. It is therefore unlikely that these substances are resulting in concerns for the environment in Canada.

7.6 Potential to cause harm to human health

7.6.1 Exposure assessment

7.6.1.1 Environmental media and food

There is a potential for the C6 alcohols to be present in water and air in limited quantities. Based on calculated results from a level III fugacity model, MIBC is expected to partition primarily to water (59.6%) and air (37.8%) with the remainder to soil (2.5%) (OECD 2005a). TMP is calculated to partition primarily to water and sediment (OECD 1990). The C6 alcohols biodegrade rapidly in aerobic, aqueous biodegradation tests and therefore are not expected to persist in aquatic environments. They are also not expected to persist in surface soils due to rapid evaporation to the air. Exposure to these C6 alcohols via environmental media is expected to be less than that from products available to consumers.

There is potential for exposure of the general population to the C6 alcohols through food. Cyclohexane and TMP have the potential for direct food contact from their potential use as components in the manufacture of food packaging materials. Although there is no definitive data on the use of cyclohexanol and MIBC as food flavouring agents in Canada, the substances are permitted in the EU as food flavouring agents for use in all categories of foods. Therefore, it is possible that cyclohexanol and MIBC are present as flavouring agents in foods sold in Canada. Exposure to the C6 alcohols from food is expected to be less than that from products available to consumers (personal communication, email from the Food Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada; December 2016, unreferenced).

7.6.1.2 Exposure from products available to consumers

Exposure scenarios were developed for the products containing C6 alcohols that lead to the greatest general population exposure.

<u>Cyclohexanol: Dermal</u>
For cyclohexanol, scenarios for dermal exposure were developed for pouring internal combustion engine cleaner (carbon removers) containing 15% cyclohexanol into the automobile. The short-term exposure of cyclohexanol for an adult weighing 70.9 kg based on 0.1 g of product exposed to the surface of the hands and assuming 100% absorption of the cyclohexanol is given in Table 8-8. Based on the assumption of a use

frequency of 6 times/year, long-term exposure to cyclohexanol from this product was not considered.

Cyclohexanol: Inhalation

There is the potential for exposure to cyclohexanol from hobby flake enamel glaze paints. Based on a specific gravity of 1.2 for the paints, the total mass of the paint is 8.9 g per container and 10% of this mass is assumed to be cyclohexanol. The exposure factors for the use of the hobby flake enamel glaze using the ConsExpo 'constant rate' model (RIVM 2007) are given in Table B-8 (Appendix B) and they result in a cyclohexanol mean concentration on the day of exposure equal to 0.20 mg/m^3. Cyclohexanol is only present in hobby paints for model kits of this type with metal flakes. Other hobby paints for model decoration do not contain this alcohol.

There is the potential for exposure to cyclohexanol from a ceramic overglaze. This is considered a specialized use as the process requires the use of a pottery kiln. Based on a specific gravity of 1.2 for the overglaze and a total mass of 8.9 g per use, with 50% of this mass is assumed to be cyclohexanol (MSDS 2017), using the ConsExpo 'constant rate' model (RIVM 2007) with the exposure factors given in Table B-9 (Appendix B), a cyclohexanol mean concentration on the day of exposure equal to 1.0 mg/m^3 was calculated.

Exposures to the alcohol component in the ceramic overglaze were estimated based on the upper limit of possible cyclohexanol concentrations given in the material safety data sheet and a ventilation rate that reflected the product labelling, which recommends use of the product in areas and kilns which are well ventilated (Duncan 2010).

MIBC

As MIBC is considered to be of low hazard potential, quantitative estimates of exposure of the general population were not derived.

TMP: Oral

For TMP, an oral exposure scenario was developed for lipstick containing 10% TMP, and a dermal scenario was developed for nail adhesive containing 10% TMP. For the lipstick oral exposure scenario for adults (70.9 kg), an ingested product amount of 0.01 g and a use frequency of 2.40 per day were used. For children (31 kg), an ingested product amount of 0.01 g and a use frequency of 0.89 per day were used.

TMP: Dermal

For dermal exposure to a nail adhesive containing 10% TMP, a use amount of 0.16 g with a use frequency of 0.2 times/day and a conservative assumption of 100% dermal absorption were used.

In summary, the short- and long-term exposure values from all sources for the C6 alcohols exposure scenarios are presented in Table 7-8.

Table 7-8. Short- and long-term systemic exposure and concentration values for consumer substances with highest exposure values

Type of exposure	% of substance in product	Exposure
Dermal	15% cyclohexanol in engine cleaner	0.21 mg/kg bw/day
Inhalation[a]	10% cyclohexanol in hobby paint 50% cyclohexanol in overglaze	0.20 mg/m^3 1.0 mg/m^3
Oral	10% TMP in lipstick (adult)[b] (child)[b]	0.034 mg/kg bw/day 0.029 mg/kg bw/day
Dermal	10% TMP in nail adhesive	0.2 mg/kg bw/day

[a] Inhalation is calculated over a 24-hour period.
[b] Applications per day for adults is 2.4 and for children is 0.89.

Cyclohexanol was not evaluated for inhalation exposure from automotive care products due to the short time consumers would be exposed to this substance from application of internal automotive engine cleaners. TMP has a low vapour pressure and volatility and is not expected to give rise to inhalation exposures.

7.6.2 Health effects assessment

The C6 alcohols in this assessment have been individually reviewed internationally for human health. These include assessment of cyclohexanol (EPA 2010; ECHA 2011; OECD 2001b), MIBC (OECD 2005a) and TMP (NIOSH 1994; OECD 1994).

None of the C6 alcohols discussed in this assessment were identified as posing a hazard to human health based on carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity classifications by other national or international agencies.

Cyclohexanol – Subchronic
In a 13-week combined repeated-dose, reproductive/developmental screening toxicity study, male and female rats were exposed to cyclohexanol at 0, 205, 614, or 1,640 mg/m^3 (6 hours/day; 5 days/week). No treatment-related signs of toxicity were observed in any dose group, and all gross, histological, biochemical or neurological endpoints appeared normal. However, prostration and decreased activity were seen in animals in the highest dose group immediately following exposure, which could be a transient effect (US EPA 2010).

In the reproductive/developmental phase of this study, male and female rats were exposed via inhalation to 0, 205, 614, or 1640 mg/m^3 of cyclohexanol through mating and gestation and up to lactation day 4. All animals were examined for reproductive and developmental parameters. Exposure to the highest dose caused a decrease in viable pups in 2 out of 11 pregnancies, and reduced mean pup body weight was seen at birth and PD 4. Converted to a daily average, the LOAEC and NOAEC were 410 mg/m^3 and 154 mg/m^3 based on litter loss and decreased pup weight, respectively. No maternal signs of toxicity were observed at the highest dose (US EPA 2010).

No oral or dermal subchronic studies were identified for cyclohexanol.

MIBC – Subchronic
In a short-term study, inhalation exposure to MIBC at 210, 826, or 3700 mg/m^3 (6 hours/day, 5 days/week) for 6 weeks caused no clinical signs of toxicity or mortality in rats, and the highest dose was identified as the NOAEC (OECD 2005a). Similarly, in a 14-week inhalation study, exposure to MIBC (209, 1043, or 4172 mg/m^3 for 6 hours/day, 5 days/week) did not cause any changes of toxicological significance in male and female rats and mice, and the highest dose (4200 mg/m^3) was considered as the NOAEC for both species (Phillips et al. 1987).

TMP – Subchronic
In a combined repeated-dose reproductive or developmental study, TMP was given at 0, 12.5, 50, 200, or 800 mg/kg bw/day via gavage) to male and female rats through mating and gestation and up to lactation day 3. There was a decrease in body weight and an increase in liver weight in male and female rats in the highest dose group (800 mg/kg bw/day), but no histopathological changes were noted. A conservative NOAEL was suggested as 200 mg/kg bw/day; however, there was an absence of any histopathological or morphological changes in liver, and no evidence of systemic or reproductive adverse effects was seen (OECD 1994).

In a 90-day repeated-dose dietary exposure study, 20, 67, 200, or 667 mg/kg bw/day of TMP was given to male and female rats. The highest dose caused an increase in liver and spleen weight and a decrease in red blood cells. In addition, a decrease in liver serum glutamic pyruvic transaminase or alkaline phosphatase activity was seen only in males at 200 mg/kg bw/day and in both sexes in the highest dose group (OECD 1994). This appears to be a non-adverse effect as alterations in hormones without evidence of histological changes may reflect adaptive changes. This is supported by another study in which 5-month dietary exposure to higher doses (1500 or 3000 mg/kg bw/day) of TMP did not cause any substance-related effects (OECD 1994). Also, no visible effects were seen on rabbit skin after dermal application of 0.5 ml (50% aqueous solution) of TMP (once a day) for 3 months (OECD 1994).

Neither cyclohexanol, MIBC, nor TMP was found to be genotoxic. No long-term or carcinogenicity studies were identified for C6 alcohols (US EPA 2010; OECD 2005a; OECD 1994).

7.6.3 Characterization of risk to human health

MIBC
In the absence of significant adverse effects in animal studies, the potential risks to human health from exposure to this substance are considered to be low.

Cyclohexanol: Dermal
As no dermal or oral studies were identified for cyclohexanol, read-across from an inhalation study was used. Assuming an inhalation rate of 16 m^3/day for an adult weighing 70.9 kg, the NOAEC of 154 mg/m^3 for reproductive effects is converted to an NOAEL exposure dose of 16 m^3/day × 154 mg/m^3 / 70.9 kg bw = 35.4 mg/kg bw/day. The systemic exposure of 0.21 mg/kg bw/day assuming 100% dermal absorption from

dermal exposure to engine cleaner gives an MOE of 165 for the day of exposure. Given the conservative nature of the 100% dermal absorption assumed for cyclohexanol and nature of the toxicological endpoints, this MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

Cyclohexanol: Inhalation

The cyclohexanol mean concentration on the day of use of hobby paint is calculated to be 0.20 mg/m^3. Using the daily adjusted NOAEC of 154 mg/cm^3 for reproductive effects gives an MOE of 770. Given the nature of the assumptions made in the exposure scenario, namely that all the paint was used in one sitting and that all inhaled cyclohexanol becomes bioavailable, and considering the nature of the toxicological endpoints, this MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

The calculated cyclohexanol mean concentration on the day of use of ceramic overglaze is calculated to be 1.0 mg/m^3. Using the daily adjusted NOAEC of 154 mg/cm^3 for reproductive effects gives an MOE of 154. Given the conservative nature of the assumptions made in the exposure scenario, this MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

TMP

For TMP, the short-term exposure doses from oral exposure from lipstick are 0.014 mg/kg bw/day for adults and 0.032 mg/kg bw/day for children. The long-term exposures to lipstick are 0.034 mg/kg bw/day for adults and 0.029 mg/kg bw/day for children. Compared to the NOAEL of 200 mg/kg bw/day for decrease in body weight, these exposures give MOEs of 14 000 and 6250 for long-term exposures to lipstick by adults and children, respectively. Given the nature and values of the toxicological endpoints, these MOEs are adequate, and the risk to the general population from exposure to TMP is considered low.

For TMP, dermal exposure to nail polish (using 100% dermal absorption) gives a short-term systemic exposure dose of 0.2 mg/kg bw. As a conservative estimate, the NOAEL of 200 mg/kg bw/day for the short-term exposure to TMP was used and with a nail polish exposure of 0.2 mg/kg bw on the day of use, an MOE of 1000 was derived. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

7.7 Uncertainties in evaluation of risk to human health

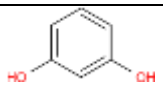
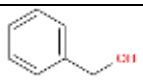
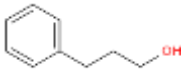
Given that the sources, uses, and properties of MIBC are well characterized, a qualitative approach to risk characterization is considered appropriate for this substance. There is some uncertainty in the exposure factors related to the use patterns of the specialty products containing cyclohexanol and TMP.

8. Aromatic alcohols

8.1 Substance identity

Information regarding the identity of the aromatic alcohols discussed in this assessment is summarized in Table 8-1 (PubChem2004-).

Table 8-1. Substance identity of the aromatic alcohols

CAS RN	DSL name (common name)	Molecular formula	Molecular structure	Molecular weight (g/mol)
108-46-3	1,3-Benzenediol (resorcinol)	$C_6H_6O_2$		110.112
100-51-6	Benzenemethanol (benzyl alcohol)	C_7H_8O		108.14
122-97-4	Benzenepropanol	$CH_{12}O$		136.194

8.2 Physical and chemical properties

Measured data for the physical and chemical properties of the aromatic alcohols is given in Table 8-2 (ChemIDplus 2017, Nair 2001). Additional physical and chemical properties data are presented in ECCC (2016b).

Table 8-2. Measured physical and chemical properties of the aromatic alcohols

Property	Resorcinol	Benzyl alcohol	Benzenepropanol
Melting point (°C)	111	−15.2	−18
Boiling point (°C)	280	205.3	235
pK_a (dimensionless)	9.32	15.4	—
log K_{ow} (dimensionless)	0.8	1.10	1.88
Water solubility (mg/L)	7.17×10^5	4.29×10^4	5.68×10^3
Vapour pressure (mmHg at 25 °C)	4.89×10^{-4}	0.094	0.0234
Henry's law constant (atm-m^3/mol)	9.88×10^{-11}	3.37×10^{-7}	2.03×10^{-7}

Benzyl alcohol and benzenepropanol are relatively more volatile than resorcinol. They all have very high water solubility and very low Henry's law constants.

8.3 Sources and uses

All three substances have been found in nature. However, production of these substances is largely from anthropogenic origins. Total manufacturing and import

volumes in Canada in 2011 as reported in response to a CEPA section 71 survey are shown in Table 8-3 (Environment Canada 2013).

Table 8-3. Summary of information on Canadian manufacturing and imports of the aromatic alcohols subgroup submitted in response to a CEPA section 71 survey

Alcohol	Total manufacture (kg)[a]	Total imports (kg)[a]
Resorcinol	1000 – 10 000	480 000
Benzyl alcohol	5000	735 000
Benzenepropanol	NR	1350

Abbreviation: NR, not reported above the DSL IU reporting threshold of 100 kg.
[a] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

Resorcinol and benzyl alcohol are largely used as solvents in industry, but all three substances are also present in a range of products available to consumers, including automotive products, household cleaning products, and construction and paint products. Resorcinol, benzyl alcohol, and benzenepropanol are used in cosmetics. The product categories and concentration ranges of the products containing aromatic alcohols with the highest exposure potential are shown in Table 8-4. The levels shown indicate concentrations of the aromatic alcohols in the formulated products and do not take into account any dilution prior to or during use. The epoxy listed as a product for benzyl alcohol is used in industrial and large-scale construction sites.

Table 8-4. Summary of Canadian products available to consumers with the highest potential for exposure to aromatic alcohols

Alcohol	Product category	Product type	Alcohol in product wt%
Benzyl alcohol	Automotive care	Fuel additive	20–30
		Automobile air freshener	5–10
	Cleaning and furnishing care	All-purpose cleaner (for grime)	5–10
		Cleaning wipes	0.5–5
		Air freshener	1–5
		Rust preventative	
	Construction or paint	Aerosol glitter paint	5
		Plasticizer	
		Epoxy glue (two tube)	1–5
		Epoxy coating for concrete floors	40–70
		Outdoors wax and finish removers	5-40
Benzenepropanol	Cleaning care	Air freshener	0.1–1

The aromatic alcohols have not been identified to be used as components in the manufacture of food packaging materials or as incidental additives used in food processing establishments in Canada. Benzyl alcohol is a food additive permitted for

use as a carrier solvent in unstandardized flavouring preparations and in one type of standardized flavouring preparation, as per the *List of Permitted Carrier or Extraction Solvents,* incorporated by reference into its respective Marketing Authorization issued under the *Food and Drugs Act*. Resorcinol, benzyl alcohol, and benzenepropanol are recognized food flavourings agents, and therefore it is possible that they are present as food flavouring agents in in foods sold in Canada (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2016; unreferenced) (see Table 8-5).

Table 8-5. Possible food uses of the aromatic alcohols in Canada[a]

Alcohol	Food packaging materials	Incidental additives[b]	Food additive	Food flavouring agent	Potential for exposure
Resorcinol	No	No	No	Yes	Yes
Benzyl alcohol	No	No	Yes	Yes	Yes
Benzenepropanol	No	No	No	Yes	Yes

[a] Personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated November 17, 2016; unreferenced.
[b] While not defined under the *Food and Drugs Act* (FDA), incidental additives may be regarded, for administrative purposes, as those substances which are used in food processing plants and which may potentially become adventitious residues in foods.

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, resorcinol, benzyl alcohol, and benzenepropanol are present in cosmetic products in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 27, 2016; unreferenced). Resorcinol is indicated as a restricted ingredient on the Cosmetic Ingredient Hotlist and is not permitted in cosmetics intended for use on the skin or in the area of the eye. The nature of the products and highest concentration of alcohol are given in Table 8-6. The concentrations show the amount of the aromatic alcohols in the formulated products and do not take into account any dilution prior to or during use.

Benzyl alcohol has been identified as a suspected sensitizer by the ECHA's Community Rolling Action Plan (ECHA 2015c). For topical use, concentrations of up to 10% in rinse-off products and up to 3% in leave-on products are permitted. EU countries and New Zealand restrict the use of benzyl alcohol in cosmetics as a preservative with a maximum 1.0 weight % in ready-for-use preparations and in other uses (other than inhibiting development of microorganisms). In Europe, the amount of benzyl alcohol must be reported in cosmetics if its concentration exceeds 0.001 weight % for leave-on products and 0.01 weight % for rinse-off products (CosIng 2018d).

Health Canada interprets section 22 of the *Cosmetic Regulations* to mean that specific cautionary statements are required when resorcinol is used in hair dyes. This interpretation of section 22 is described in the Hotlist entry for resorcinol.

Table 8-6. Cosmetics in Canada containing the aromatic alcohols

Alcohol	Number of cosmetic products where substance is found	Products and maximum stated concentration	Conditions of use	Cosmetic Ingredient Hotlist
Resorcinol	2160 products	2150 hair products – 10% 1 non-permanent makeup (eye/face use) – 3%	Permitted in hair dyes with warning	Described as a restricted ingredient. Not permitted in cosmetics for use on skin. Additionally, limitations similar to coal tar dye for hair dyes apply.
Benzyl alcohol	12 050 products	Antiperspirants – 20% Bath products – 10% Eyeliner – 30% Eye/face cleanser – 19% Hair bleach/colour – 30% Hairstyling product – 30% Hair conditioner – 10% Makeup – 10% Makeup remover – 1% Moisturizer – 30% Nail polish/remover – 3% Shampoo – 10% Toothpaste – 3%	N/A	N/A
Benzene-propanol	205 products	Hand lotion, foot cream – 10% Hair products – 3% Makeup – 3% Moisturizer – 1%	N/A	N/A

Abbreviation: N/A, not applicable

The uses of the aromatic alcohols in NHPs in Canada are summarized in Table 8-7.

Table 8-7. NHP uses of the aromatic alcohols in Canada

Alcohol	NHPID	LNHPD	Comments
Resorcinol	Yes	Yes	- Medicinal role as classified as an NHP substance falling under Schedule 1, item 2 (an isolate) to the NHPR - Present in currently licensed NHPs
Benzyl alcohol	Yes	Yes	- Medicinal role as classified as an NHP substance falling under Schedule 1, item 2 (an isolate) to the NHPR - Non-medicinal role for use as flavour enhancer, fragrance ingredient, preservative antimicrobial, or solvent. For topical use as non-medicinal ingredient, up to 10% in rinse-off products and up to 3% in leave-on products - Acceptable daily intake up to 5 mg/kg bw/day, expressed as benzoic acid equivalents - Must be declared as medicinal ingredient in throat lozenges in daily doses at or above 100 mg/day and in anorectal products in concentrations at or above 1% w/w - Present in currently licensed NHPs
Benzenepropanol	Yes	Yes	- Non-medicinal role for oral use as flavour enhancer and topical use as fragrance ingredient, masking agent, or solvent - Present in currently licensed NHPs

Abbreviations: NHP, natural health product; NHPID, Natural Health Products Ingredients Database; LNHPD, Licensed Natural Health Products Database; NHPR, *Natural Health Products Regulations*

[a] Personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated October 26, 2016; unreferenced.

Benzyl alcohol appears as a non-medicinal ingredient in non-prescription drugs, such as surface disinfectants, sinus sprays, pain creams, sunscreens, mouthwash, antifungals, and antidandruff shampoo. It is also a non-medicinal ingredient in a number of prescription drugs with primarily intravenous administration (personal communication, email from the Natural and Non-prescription Health Products Directorate and Therapeutic Products Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated April 30, 2021, and May 23, 2019; unreferenced).

Benzyl alcohol is found in pest control products as a formulant (PMRA 2010).

In addition, resorcinol has been detected in honey mushrooms, in tobacco leaves in small amounts, and in cane molasses (OECD 2009; WHO 2006). Benzyl alcohol can be derived from many plants, fruits, teas, and essential oils, including jasmine, hyacinth,

and ylang-ylang (Merck Index 2010). Benzenepropanol occurs in resins, balsams, cinnamon, and a variety of fruits, berries, and mushrooms (PubChem 2004-). Resorcinol and benzenepropanol are also found in alcoholic beverages.

Benzyl alcohol has been identified as a flavourant in vaping products (Tierney et al. 2015; Czoli et al. 2019; Krüsemann et al. 2021). Vaping products (also known as electronic cigarettes) may represent an additional source of exposure to these substances. The assessment of risk to the general population from this use, including risk relative to that associated with conventional cigarettes, and possible options to mitigate risk associated with these products are being addressed through a separate legislative framework (Health Canada [modified 2020]).

8.4 Environmental fate and behaviour

In terms of environmental fate, the aromatic alcohols have high to very high mobility in soil. Volatilization of these substances from moist soil surfaces is not expected to be an important fate process, nor is volatilization from water surfaces.

8.4.1 Environmental persistence

Similar to all phenols, the aromatic alcohols are expected to react relatively rapidly in sunlit natural water via reaction with photochemically produced hydroxyl radicals and peroxy radicals. According to models used in ERC (ECCC 2016b), the aromatic alcohols are not expected to persist in air, water, sediment, or soil.

8.4.2 Potential for bioaccumulation

Given their low log K_{ow} and low bioconcentration factors (ECCC 2016b), the aromatic alcohols are not expected to significantly bioaccumulate in organisms.

8.5 Potential to cause ecological harm

8.5.1 Characterization of ecological risk

The ecological risks of the aromatic alcohols have been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profiles for the aromatic alcohols, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

The hazard and exposure classifications for the aromatic alcohols are summarized in Table 8-8.

Table 8-8. Ecological risk classification results for the aromatic alcohols

Substance	ERC hazard classification	ERC exposure classification	ERC risk classification
Resorcinol	low	low	low
Benzyl alcohol	low	low	low
Benzenepropanol	low	low	low

On the basis of low hazard and low exposure classifications according to information considered under ERC, resorcinol, benzyl alcohol, and benzenepropanol were classified as having a low potential for ecological risk. It is therefore unlikely that these substances are resulting in concerns for the environment in Canada.

8.6 Potential to cause harm to human health

8.6.1 Exposure assessment

8.6.1.1 Environmental media and food

Level III fugacity model results indicate that the aromatic alcohols partition primarily to water and soil (OECD 2008; OECD 2001c). The aromatic alcohols biodegrade rapidly in aerobic, aqueous biodegradation tests and therefore would not be expected to persist in aquatic and soil environments. Exposure to the aromatic alcohols via environmental media is therefore expected to be low.

None of the aromatic alcohols have been identified as used as components in the manufacture of food packaging materials nor in incidental additives used in food processing establishments in Canada. Resorcinol, benzyl alcohol, and benzenepropanol naturally occur in certain foods, and are potentially present as food flavourings agents in foods sold in Canada. Benzyl alcohol is also permitted for use as a food additive in Canada for the purpose of a carrier solvent in certain flavouring preparations, as per the *List of Permitted Carrier or Extraction Solvents,* incorporated by reference into its respective Marketing Authorization issued under the *Food and Drugs Act*.

A comparison of production volumes suggests that exposure to benzyl alcohol from its use as food flavouring is expected to be greater than exposure from foods that naturally contain benzyl alcohol (JECFA 2002). Therefore, exposure from this source is further quantified. Internationally, JECFA evaluated benzyl alcohol as a food flavouring agent and estimated the corresponding per capita intake of benzyl alcohol at 17 000 µg/day (290 µg/kg bw per day) for the US population (International Organization of the Flavor Industry 1995; Lucas et al. 1999, both cited in JECFA 2002; IPCS 2005). Based on the available information, the per capita intake derived by JECFA for benzyl alcohol is a conservative estimate of possible Canadian dietary exposure from all food flavouring-related uses of this substance, including its use as a flavouring agent and as a carrier solvent (food additive) in flavouring preparations in the general population 1 year of age and older (personal communication, email from Food Directorate, Health Canada to

Existing Substances Risk Assessment Bureau, Health Canada, 2018; unreferenced). Exposure to these substances from food uses is expected to be less than that from uses of certain products available to consumers.

8.6.1.2 Exposure from products available to consumers

As shown in Table 9-5, the aromatic alcohols are found to varying extent in Canadian products available to consumers.

Resorcinol
Only dermal exposures were identified from products available to consumers.

The use of hair dye results in the largest dermal exposure to resorcinol. A scenario where resorcinol is used in permanent hair colour at a concentration of 10%, at a use frequency of 0.02 per day, with a product amount of 100 g, and assuming a dermal absorption of 10% for an adult results in a systemic exposure of 1.4 mg/kg bw/day.

Benzyl alcohol
Oral exposure
In their use as NHPs and non-prescription drugs in throat lozenges, benzyl alcohol must be declared as a medicinal ingredient at daily doses at or above 100 mg/day. This is consistent with the analgesic/anaesthetic properties of benzyl alcohol and its presence at quantities per lozenge of 100 to 500 mg in the Natural and Non-prescription Health Products Directorate's Throat Lozenges monograph (Health Canada 2018; NHPID 2021). In a number of throat lozenges retrieved from a search of publicly available databases, the amount of benzyl alcohol declared as non-medicinal ingredient is given on the packaging as 5.0 to 6.5 mg per lozenge. A maximum use of 12 lozenges per day results in a maximum daily dose of 78 mg/day, which leads to an oral exposure of 1.1 mg/kg bw/day for an adult weighing 70.9 kg and 1.3 mg/kg bw/day for a teenager weighing 59.4 kg.

Oral exposure to benzyl alcohol may also arise from the use of cosmetics, NHPs, and non-prescription drugs formulated as lip balm, toothpaste, and mouthwash. Exposures from products with the highest concentration of benzyl alcohol are summarized in Table 8-9 with exposure factors given in Table B-10 (Appendix B).

Table 8-9. Oral exposures to benzyl alcohol from cosmetics, NHPs, and non-prescription drugs

Product	Age group	Calculated dose (mg/kg bw/day)
Lip balm	9–13 to 19+	0.010 to 0.012
Toothpaste	2–3 to 19+	0.068 to 0.27
Mouthwash	4–8 to 19+	0.72 to 0.86

Dermal exposure
An *in vivo* study of dermal absorption of benzyl alcohol and other benzyl derivatives was carried out on the skin of rhesus monkey which was shown to resemble human skin in

terms of absorption properties of the benzyl derivatives. The dermal absorption percent of benzyl alcohol on unoccluded abdominal skin was determined to be 32 ± 4% (Bronaugh et al. 1990). An *in vitro* study has been carried out to determine the evaporation and dermal absorption of benzyl alcohol (from a 1% solution in ethanol) exposed to human skin samples under different conditions of airflow above the sample (Saiyasombati and Kasting 2003). Based on the airflow, dermal absorptions of benzyl alcohol of between 48% (low airflow) and 12% (high airflow) of the applied dose were measured. Considering these studies, a 50% dermal absorption was applied for benzyl alcohol in this assessment.

The highest dermal exposure to benzyl alcohol from NHPs and non-prescription drugs is from the use of sunscreen lotion, which is considered as the sentinel product. For sunscreen lotion, the amount used by adults and children aged 2 to 3 years is taken to be 12 g/day and 3 g/day, respectively. For an adult user weighing 70.9 kg and a 2- to 3-year-old infant weighing 15.5 kg, a scenario assuming a benzyl alcohol concentration in sunscreen at 1.74% and a dermal absorption of 50% gives systemic exposures of 1.4 mg/kg bw/day and 1.7 mg/kg bw/day, respectively.

Systemic exposures to benzyl alcohol from dermal contact through the use of a wash-off face cleanser are presented in Table 8-10. The exposure factors used in these calculations are given in Table B-11 of Appendix B.

Table 8-10. Systemic exposures to benzyl alcohol from NHPs

Product	Age group (year)	Maximum weight %	Systemic exposure (mg/kg bw/day)
Sunscreen	2–3 to 19+	1.74	1.4 to 1.7
Face cleanser	4–8 to 19+	19	0.015 to 0.029

Systemic exposures for different age groups from dermal contact with cosmetic products containing benzyl alcohol found in Canada were determined and are presented in Table 8-11. The exposure factors used in these calculations are given in Table B-12 of Appendix B.

Table 8-11. Systemic exposures to benzyl alcohol from cosmetic products (dermal absorptions of 0.5 are used in the calculations)

Product	Age group	Maximum weight %	Systemic exposure (mg/kg bw/day)
Body cream/moisturizer	0–5 months to 19+ years	30	159 to 68
Deodorant/antiperspirant	9–13 to 19+ years	20	1.0 to 1.7
Eye makeup remover	4–8 to 19+ years	1	0.011 to 0.002
Face cream	9–13 to 19+ years	10	1.2 to 2.0
Face makeup/foundation	4–8 to 19+ years	10	0.74 to 0.33
Fragrance	2–3 to 19+ years	3	0.28 to 0.10

Shampoo	0–5 months to 19+ years	10	0.31 to 0.08
Massage oil	6–11 months to 19+ years	1	0.99 to 0.22
Nail polish remover	2–3 to 19+ years	3	0.76 to 0.46

The highest dermal exposure to benzyl alcohol from household products available to consumers is from the use of an all-purpose grime cleaner containing up to 10% benzyl alcohol. A dermal exposure scenario was calculated for this product using exposure factors from ConsExpo Web (RIVM 2018) given in Table B-13 (Appendix B). It is assumed that 2.9 g of the cleaner (0.29 g benzyl alcohol) comes in contact with the skin. This scenario leads to conservative estimates for a short-term exposure internal dose of 0.2 mg/kg bw for the day of exposure and a long-term exposure dose of 0.11 mg/kg bw/day.

Inhalation Exposure
Inhalation exposure to benzyl alcohol vapour from the application of all-purpose spray cleaner was calculated using the ConsExpo Web exposure factors given in Table B-14 (Appendix B). Using these assumptions, the peak concentration and mean concentration on the day of exposure are calculated to be 0.099 mg/m^3 and 0.016 mg/m^3, respectively. The systemic exposure on the day of exposure is 0.0038 mg/kg bw.

Inhalation exposure to benzyl alcohol vapour from the use of liquid air freshener was calculated using the ConsExpo Web constant rate scenario as a conservative estimate. The liquid product is 5.5 mL, 1.02 specific gravity, contains 5% weight benzyl alcohol, with total use duration of the product being given as 30 days. The exposure factors for this scenario from ConsExpo (RIVM 2018) are given in Table B-15 (Appendix B). Using these assumptions, the peak concentration and mean concentration on the day of exposure are calculated to be 3.8 µg/m^3 and 0.21 µg/m^3, respectively. The systemic exposure on the day of exposure is 0.66 µg/kg bw/day.

A two-part epoxy shield coating product containing benzyl alcohol is used on concrete surfaces (MSDS 2010b). This product is expected to be used by professionals or individuals in empty rooms, usually garages or basements. The ConsExpo “exposure to vapour: constant rate” scenario for a general coating, with exposure factors given in Table B-16 (Appendix B) were used to determine inhalation exposure from this use. This scenario gave a mean benzyl alcohol concentration on the day of exposure of 10 mg/m^3. Using a breathing rate of 14.4 m^3/day light exercise (activity) and an average adult weight of 70.9 kg gives an exposure dose of 2.1 mg/kg bw/day. This exposure scenario is considered to provide an upper bound to the benzyl alcohol exposures from other construction or specialty paint products.

<u>Benzenepropanol</u>
Dermal exposure

Bhatia et al. (2011) calculated the total skin exposure to benzenepropanol used as a fragrance in 10 cosmetic products, including body lotion, face cream, shampoo, and bath products, among others. To generate a conservative estimate, from the survey of several thousand products, they determined the 97.5th percentile of the benzenepropanol component in the fragrance used in each product and used the 97.5th percentile in each of the 10 products. Based on the nature of the product, in particular the length of time the product was expected to remain on the skin and whether the fragrance would be rinsed off, they applied retention factors of 0.001 to 1.0 to the benzenepropanol component. The high usage body lotion and fragrance cream products were assigned a retention factor of 1.0. Using the exposure factors for fragrances (Ford et al. 2000; Cadby et al. 2002), the total estimated systemic exposure to benzenepropanol from these products was determined to be 0.0204 mg/kg bw/day for a 60-kg adult, the majority of this exposure being from perfume (0.008 mg/kg bw/day) and body lotion (0.003 mg/kg bw/day).

An *in vitro* study on rat skin samples has been carried out to determine the evaporation and dermal absorption of benzenepropanol from 75% saturated (S = 6.68 mg/ml) solutions in buffer at pH 6.2 (Lopez 1998). The solution on the skin samples was replenished every 30 minutes to keep a constant degree of saturation on the skin samples. In all samples, dermal absorptions of benzenepropanol were less than 10%. The authors determine a permeability coefficient of K_p = 0.130 cm/h for benzenepropanol. A maximum flux model can be used for this substance using the following formula:

$$\text{Maximum flux} = Kp \times S = 0.130 \times 0.130 = 0.87 \text{ mg/(cm}^2\cdot\text{h)}$$

The highest exposure to benzenepropanol from cosmetic products available in Canada is from foot cream and hand lotion with 10 weight % benzenepropanol content. This concentration is significantly above the saturation concentration of benzenepropanol. Assuming the daily use of the foot cream product over a 1170 cm^2 area of the feet with 1-hour exposure time for adults (weighing 70.9 kg) and teenagers (weighing 59.4 kg), the long-term exposures to benzenepropanol are determined to be 0.60 mg/kg bw/day and 0.71 mg/kg bw/day, respectively. Assuming twice daily use of the hand lotion product over a 860 cm^2 area of the hands with 1-hour exposure time, the long-term systemic exposures to benzenepropanol from hand lotion are determined to be 0.88 mg/kg bw/day and 1.02 mg/kg bw/day, respectively.

Given the benzenepropanol percent distribution in body moisturizer products, there are products with composition of 1% benzenepropanol. This concentration is near the saturation concentration of benzenepropanol and this is depleted as some of the substance is absorbed into the skin. Therefore, the maximum flux method was not used for this exposure. Assuming product use of 12 g and 10.4 g for adults and teens, respectively, based on 10% dermal absorption, the systemic exposures for adults and teenagers are 0.169 mg/kg bw/day and 0.174 mg/kg bw/day, respectively.

In NHPs, benzenepropanol is used as a non-medicinal ingredient in products including lotions and sunscreens with maximum percentages reported to be 0.6% (LNHPD 2021; NHPID 2021). Exposures to these products are assumed to be less than the cosmetic products quantitatively considered above.

8.6.2 Health effects assessment

Aromatic alcohols have been individually reviewed internationally for human health and ecological risk. These include assessments of resorcinol (ECHA 2011 [updated 2017]; OECD 2008; /IPCS 2006; NTP 1992), benzyl alcohol (EC 2002; CIR 2001; OECD 2001; NTP 1989) and benzenepropanol (ECHA 2017c). These reviews, as well as some primary literature, were used to inform the health effects characterization in this assessment. This comprehensive set of reliable test data in various animals allows for read-across of some non-tested components of this assessment. All studies described herein pertain to the substances described in this assessment.

None of the aromatic alcohols in this assessment were identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity.

Resorcinol (CAS RN 108-46-3)

Resorcinol may cause skin sensitization (IPCS 2006).

In a subchronic (13-week) dose-finding study, male and female F344 rats or B6C3F1 mice were given resorcinol via gavage in drinking water for 5 days/week at 32, 65, 130, 260, or 520 mg/kg bw/day in rats and 28, 56, 112, 225, or 420 mg/kg bw/day in mice. The authors reported that nearly all rats and mice in the highest dose group (520 mg/kg bw/day or 420 mg/kg bw/day) died within the first 7 to 14 days because of an acute toxic reaction. At non-lethal doses, the only change observed was a slight or scattered increase in liver or adrenal weight in both species and sexes that was not considered biologically significant by the authors as no changes were seen in biochemical, gross or microscopic parameters in resorcinol-treated rats when compared to controls (NTP 1992).

In a two-generation reproductive study, administration of 120, 360, 1000, or 3000 mg/L of resorcinol via drinking water in male and female rats did not cause treatment-related systemic, parental, or reproductive effects in any dose group. The highest dose (3000 mg/L) was equivalent to a NOAEL of 233 mg/kg bw/day (male) and 304 mg/kg bw/day (female) during premating and gestation and a NOAEL of 660 mg/kg bw/day was reported for female rats during the lactation period (RTF 2005). In a developmental study, exposure to resorcinol (dissolved in propylene glycol) 125, 250, or 500 mg/kg bw/day via gavage in rats (GD 6 to 15) did not cause any adverse effects on the developing fetuses or dams, and the highest dose was considered as a NOAEL (DiNardo 1985).

Resorcinol was generally negative in most genotoxicity assays including the Ames bacterial mutation assay, unscheduled DNA synthesis assay, thymidine kinase locus study, hamster embryo morphological transformation assay, micronucleus assay, and RasH2 assay (OECD 2008). EFSA (2010) established an ADI of 0.12 mg/kg bw/day for resorcinol based on a NOAEL of 50 mg/kg bw/day for acute neurological signs (ataxia, prostration, salivation and tremors) that disappeared within 30to 60 minutes of ingestion of resorcinol in male and female rats. EFSA obtained this NOAEL from a NTP carcinogenicity study in which resorcinol was given (gavage in drinking water) at 0, 112, or 225 mg/kg bw/day to male and 0, 50, 100, or 150 mg/kg bw/day to female rats for 5 days/week for 2 years (NTP 1992). This NOAEL was further adjusted to 36 mg/kg bw/day by EFSA in order to account for a 7-day exposure week from a 5-day dosing week. EFSA considered it as a conservative approach to take into account the dietary exposure to resorcinol in adult or children who may consume raw shrimp, which may contain above 35 mg/kg of resorcinol (EFSA 2010).

Benzyl alcohol (CAS RN 100-51-6)

In a 13-week repeated-dose study, benzyl alcohol was administered (gavage/corn oil) at 50, 100, 200, 400, or 800 mg/kg bw/day to male and female rats for 5 days/week (NTP 1989). The highest dose caused signs of neurotoxicity, including staggering, laboured breathing and lethargy, along with a decrease in body weight in both male and female rats. Post-mortem examination revealed necrosis of dentate gyrus or hippocampus of brain, skeletal muscle necrosis, and thymic atrophy and congestion in both sexes in the highest dose group. Reduced body weight in female rats was observed at a dose of 400 mg/kg bw/day but not at the dose of 800 mg/kg bw/day (NTP 1989).

The US EPA also examined the NTP (1989) study and proposed a subchronic (13-week) or chronic (2-year) oral RfD of 1.0 mg/kg bw/day or 0.3 mg/kg bw/day, respectively, after amortization of dosing from 5 days/week to 7 days/week for exposure. The US EPA considered an amortized NOAEL for seven days/week exposure of 143 (based on a 5 day/week dosing of 200) mg/kg bw/day based on decrease in body weight in female rats and a LOAEL of 286 (400) mg/kg bw/day based on hyperplasia of forestomach in male rats (US EPA 2009). These effects do not appear adverse as a decrease in body weight of female rats in various dose groups was not dose-related and the proliferation of forestomach epithelium is known to occur due to tissue irritation from gavage dosing (for 2 years). Since the time of the US EPA review, it has been suggested that proliferative lesions in rat forestomach should not be considered relevant to human unless a human relevant dose was used or there was development of tumours at multiple sites, or if a chemical had a genotoxic mode of action (Proctor et al. 2007).

For these reasons, in this assessment, a NOAEL of 400 mg/kg bw/day and a LOAEL of 800 mg/kg bw/day were identified, as changes in body weight did not appear to be dose related.

Benzyl alcohol showed equivocal evidence for sensitization in experimental animals and humans. No mutagenicity was observed and the genotoxicity or carcinogenicity potential of benzyl alcohol was considered negative (OECD 2001; JECFA 1996).

Benzyl alcohol is metabolized to benzoic acid in the human body, and some aspects of the hazard may be related to this metabolite (EC 2002).

Benzenepropanol (CAS RN 122-97-4)

Limited health effects data was identified for benzenepropanol. In a combined repeated-dose reproductive/developmental toxicity study, male and female rats were given 0, 100, 300, or 1000 mg/kg bw/day of benzenepropanol via gavage (in corn oil) 14 days prior to mating, through the mating (male and female) and gestation, and up to lactation day 13. No maternal clinical signs of toxicity or compound-related gross or histopathological changes were seen in any treatment group. The highest tested dose of 1000 mg/kg bw/day was considered as a NOAEL for maternal systemic toxicity. An increased number of dead or cannibalized pups and a decrease in body weight gain in F_1 pups (from 1000 mg/kg bw/day dams) were observed on PND 4 (94%) and PND 13 (92%). The increase in dead pups was due to loss of one whole litter affecting 20 pups; other litters were not affected. The authors reported a NOAEL of 300 mg/kg bw/day for reproductive and developmental effects (ECHA 2017).

Exposure to benzenepropanol is not known to cause any adverse effects in human volunteers following dermal exposures up to a concentration of 8% for 48 hours (RIFM 1976b).

Benzenepropanol was not mutagenic in the tested strains (RIFM 2002).

8.6.3 Characterization of risk to human health

Resorcinol

Dermal exposure to resorcinol from the use of hair dye was determined to lead to a systemic exposure of 0.031 mg/kg bw/day. Compared to the NOAEL of 233 mg/kg bw/day (highest dose tested) for a two-generational reproductive/developmental study on rats, this exposure gives an MOE of 7500. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

Benzyl alcohol

Oral

The maximum allowed daily dose of benzyl alcohol in throat lozenges as a non-medicinal ingredient is 100 mg/day. The total daily dose of benzyl alcohol from lozenges in the market is 78 mg/day. This leads to exposures of 1.1 mg/kg bw/day for adults and 1.3 mg/kg bw/day for teenagers. A 13-week repeated-dose gavage study on rats resulted in a NOAEL of 400 mg/kg bw/day for neurotoxicity. This gives a MOE of 307 for oral exposure to benzyl alcohol from lozenges for teenagers. This MOE is considered adequate to account for uncertainties in exposure and health effects.

JECFA estimated the per capita intake of benzyl alcohol as a food flavouring agent at 290 µg/kg bw/day. Compared to the NOAEL of 400 mg/kg bw/day for neurotoxicity from a 13-week repeated-dose gavage study, this gives a MOE of 1380. This MOE is considered adequate to account for uncertainties in exposure and health effects. The estimated exposure is also lower than the upper bound of the acceptable daily intake (ADI) of 5 mg/kg bw/day established by JECFA for benzoic acid, the benzoate salts, benzaldehyde, benzyl acetate and benzyl alcohol, expressed as benzoic acid equivalents (JECFA 2002). Therefore, the risk to the general population 1 year of age and older from oral exposure to benzyl alcohol in food flavouring agents, which includes its use as a carrier solvent (food additive) in flavouring preparations, is considered to be low.

The oral exposures to other products in the NHPs and non-prescription drugs categories, including lip balm, mouthwash, and toothpaste, are in the range of 0.010 mg/kg bw/day to 0.86 mg/kg bw/day. Using the NOAEL of 400 mg/kg bw/day for neurotoxicity gives MOEs of 40 000, 985, and 465 for lip balm, toothpaste, and mouthwash exposure, respectively. These MOEs are considered adequate to address the uncertainties in the exposure and health effects databases.

Dermal

Using the estimated ranges of 50% dermal absorption, the systemic exposures to benzyl alcohol from the use of sunscreen lotion (at 1.74%) were determined to be 1.4 for adults and 1.7 mg/kg bw/day for 2- to 3-year-old infants. Using the NOAEL of 400 mg/kg bw/day for neurotoxic effects from a 13-week oral study on rats gives MOEs of 285 for adults and 235 for infants. Due to the severity and non-reversible nature of the effects, the lack of chronic neurotoxicity data, and the possibility of long-term exposure to the sunscreen product, these MOEs are considered potentially inadequate to account for uncertainties in exposure and health effects databases.

The systemic exposures to benzyl alcohol from the use of face cleanser for children, teens, and adults ranged from 0.015 mg/kg bw/day to 0.029 mg/kg bw/day. Using the NOAEL of 400 mg/kg bw/day gives MOEs ranging between 14 000 and 27 000, which are considered adequate to address the uncertainties in the exposure and health effects databases.

The systemic exposures to benzyl alcohol from the use of cosmetic products for different age groups given in Table 8-11 are compared to the NOAEL of 400 mg/kg bw/day to give the MOEs presented in Table B-17 (Appendix B). The MOEs for the body cream/moisturizer, deodorant/antiperspirant, and face cream categories are provided in Table 8-12 and are not considered adequate to address the uncertainties in the exposure and health effects databases.

Table 8-12. Systemic exposures and MOEs for benzyl alcohol in cosmetic products

Product	Age group (months/years)	MOE
Body cream/moisturizer	0–5 months to 19+ years	2.5 to 5.9

Deodorant/antiperspirant	9–13 year to 19+ years	240 to 400
Face cream	9–13 year to 19+ years	197 to 330

The use of benzyl alcohol in all-purpose surface grime cleaners leads to an exposure of 0.11 mg/kg bw/day. Using the NOAEL of 400 mg/kg bw/day gives an MOE of 3600. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

Inhalation
The inhalation exposure to benzyl alcohol from the use of all-purpose cleaner was determined to be 3.8 µg/kg bw/day for the day of exposure. Using the NOAEL of 400 mg/kg bw/day for neurotoxic effects from a 13-week oral study on rats gives an MOE of 10 500. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

The inhalation exposure to benzyl alcohol from the use of liquid air freshener was determined to be 0.66 µg/kg bw/day for the day of exposure. Using the NOAEL of 400 mg/kg bw/day for neurotoxic effects from a 13-week oral study on rats gives an MOE of 600 000. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

The inhalation exposure to benzyl alcohol from the application of epoxy shield coating was determined to be 2.1 mg/kg bw/day for the day of exposure. Using the NOAEL of 400 mg/kg bw/day for neurotoxic effects from a 13-week oral study on rats gives an MOE of 190. Based on the expected intermittent and/or limited duration of exposure, this MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

<u>Benzenepropanol</u>
As the effects of concern are considered reproductive and/or developmental, the target population are those of reproductive age, specifically adults and teenagers. The NOAEL of 300 mg/kg bw/day was used to determine MOEs for the exposure of this subpopulation to benzenepropanol.

The systemic exposures to benzenepropanol from the use of foot cream and hand lotion containing 10% of this product by teenagers were determined to be 0.71 and 1.04 mg/kg bw/day, respectively. Using the NOAEL of 300 mg/kg bw/day, MOEs of 420 and 290 were derived for the exposure of teens to benzenepropanol from the use of foot cream and hand lotions, respectively. These MOEs are considered adequate to address the uncertainties in the exposure and health effects databases.

For a content of 1% benzenepropanol in moisturizer, the systemic exposure doses for adults and teenagers are 0.17 mg/kg bw/day, with a corresponding MOE of 1700. This MOE is considered adequate to address the uncertainties in the exposure and health effects databases.

The risks posed by exposure to products mentioned above is considered to provide an upper bound for other cosmetic and NHP products available in Canada.

8.7 Uncertainties in evaluation of risk to human health

There are uncertainties in the dermal absorption of benzyl alcohol and benzenepropanol. A conservative estimate of the absorption of 10% has been used, which was the value for the unventilated conditions for the *in vitro* study.

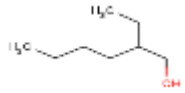
There is uncertainty in the benzyl alcohol and benzenepropanol content of some of the products available to consumers. There is a significant range of concentrations reported on the products, and more precise knowledge of the concentration would remove some uncertainty in the MOEs. Furthermore, there are a large number of products that contain these substances, which may result in higher exposure, thus contributing to uncertainty.

9. 2-Ethyl-1-hexanol

9.1 Substance identity

Information regarding the identity of 2-ethyl-1-hexanol is summarized in Table 9-1 (PubChem 2004-).

Table 9-1. Substance identity of 2-ethyl-1-hexanol

CAS RN	DSL name (common name)	Molecular formula	Chemical structure	Molecular weight (g/mol)
104-76-7	1-Hexanol, 2-ethyl (2-ethyl-1-hexanol)	$C_8H_{18}O$		130.23

9.2 Physical and chemical properties

Measured data for the physical and chemical properties of 2-ethyl-1-hexanol are given in Table 9-2 (ECHA 2018b, PubChem 2004-). Additional physical and chemical properties are presented in ECCC (2016b).

Table 9-2. Measured physical and chemical properties of 2-ethyl-1-hexanol

Melting point (°C)	Boiling point (°C)	log K_{ow} (dimensionless)	Water solubility (mg/L)	Vapour pressure (Pa)
-89	184–186	2.9 at 25 °C	900 at 20 °C	93 at 20 °C

This substance is expected to volatilize from water surfaces.

9.3 Sources and uses

2-Ethyl-1-hexanol is naturally present in corn, olive oil, tea, rice, tamarind, grapes, blueberries, and other foods.

No Canadian manufacture value was submitted for 2-ethyl-1-hexanol in 2011 in response to a CEPA section 71 survey (Environment Canada 2013). A total import volume of 33 000 000 kg was reported in this survey.[7]

The uses reported in response to a CEPA section 71 survey (Environment Canada 2013) include as a finishing agent, fuel and fuel additive, lubricant and grease, building and construction material, solvent, adhesive, sealant, and cleaning agent, as well as in oil and gas extraction. The majority of the uses of this substance are in industrial applications, primarily as an emollient and plasticizer.

According to notifications submitted under the *Cosmetic Regulations* to Health Canada, 2-ethyl-1-hexanol is not found in any cosmetic products in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 27, 2016; unreferenced). It is not included on the Cosmetic Ingredient Hotlist (Health Canada 2018).

As shown in Table 9-3, 2-ethyl-1-hexanol may be used as a component in the manufacture of food packaging materials in Canada and does have potential for direct food contact and exposure (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated December 2016). It is known to be used internationally as a food flavouring agent. Therefore, it is possible that the substance is present as a food flavouring agent in foods sold in Canada.

This substance is listed in the Natural Health Products Ingredients Database (NHPID) with a non-medicinal role for oral use only as flavour enhancer, as well as with an acceptable daily intake of 0.5 mg/kg bw/day based on JECFA (1997).

Table 9-3. Possible uses of 2-ethyl-1-hexanol in foods in Canada[a]

Food packaging material	Incidental additives[b]	Food additive	Food flavouring agent	Potential for exposure
Yes (in plasticizer of PVC film)	No	No	Yes	Yes

[a] Personal communication, from Health Canada Food Directorate to Health Canada Risk Management Bureau, dated December 2016

[7] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

[b] While not defined under the *Food and Drugs Act* (FDA), incidental additives may be regarded, for administrative purposes, as those substances which are used in food processing plants and which may potentially become adventitious residues in foods.

Products available to consumers which contain this substance are given in Table 9-4 and are all in the category of automotive care products.

Table 9-4. 2-Ethyl-1-hexanol in Canadian products available to consumers[a]

Product Category	Product Type	Weight % in Product
Automotive care	Engine cleaner; fuel enhancer	1–10

[a] MSDS 2008, 2011, 2014d, 2014e, 2015d.

2-Ethyl-1-hexanol is found in pest control products (PMRA 2010), as a formulant.

9.4 Environmental fate and behaviour

9.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), 2-ethyl-1-hexanol is not expected to persist in air, water, sediment, or soil (ECCC 2016b).

9.4.2 Potential for bioaccumulation

Given its low log K_{ow} and low bioconcentration factor (ECCC 2016b), 2-ethyl-1-hexanol is not expected to significantly bioaccumulate in organisms.

9.5 Potential to cause ecological harm

9.5.1 Characterization of ecological risk

The ecological risk of 2-ethyl-1-hexanol has been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profiles for 2-ethyl-1-hexanol, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

On the basis of low hazard and low exposure classifications according to information considered under ERC, 2-ethyl-1-hexanol was classified as having a low potential for ecological risk. It is therefore unlikely that this substance is resulting in concerns for the environment in Canada.

9.6 Potential to cause harm to human health

9.6.1 Exposure assessment

9.6.1.1 Environmental media and food

Exposures to this substance from environmental media and food are expected to be limited and less than that from use of certain products available to consumers.

9.6.1.2 Exposure from products available to consumers

A scenario using thin film exposure to automotive products that contain 2-ethyl-1-hexanol is used to estimate the dermal exposure (US EPA 2011b). The surface area of the fingertips (6 cm^2) is assumed to be exposed to the product with a film thickness of 0.016 cm. The density of automotive products is approximately 0.9 g/cm^3 with a maximum of 10% of the product being 2-ethyl-1-hexanol. With 100% dermal absorption, this leads to a short-term systemic exposure of 0.12 mg/kg bw/day on the day of exposure.

9.6.2 Health effects assessment

2-Ethyl-1-hexanol has not been reviewed internationally and has not been identified as posing a hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity.

Subchronic (90-day gavage) administration of 0, 25, 125, 250, or 500 mg/kg bw/day of 2-ethyl-1-hexanol did not cause toxicity at low doses. However, exposure to 250 mg/kg bw/day caused a decrease in serum alkaline phosphatase (AP) and glucose in male rats and a decrease in serum alanine aminotransferase (ALT) in female rats along with an increase in liver weight in both sexes. The highest dose (500 mg/kg bw/day) caused a significant decrease in body weight gain, serum ALT, glucose and cholesterol levels in male and female rats. There was an increase in reticulocytes, AP and serum protein and albumin levels both sexes. Also, an increase in relative liver, stomach or brain weight was reported in both sexes (BASF 1992). The LOAEL of 250 mg/kg bw/day can be considered for a decrease in serum AP.

In a developmental study, pregnant rats were orally administered (gavage) a single dose of 800 or 1600 mg/kg bw/day of undiluted 2-ethyl-1-hexanol on GD 12. Controls received no gavage (untreated). Exposure to 1600 mg/kg bw/day of 2-ethyl-1-hexanol caused a significant increase in the number of malformed pups which showed hydronephrosis and tail or limb defects. However, no maternal toxicity, pup deaths or fetal resorptions were present (Ritter 1986, 1987). In mice, developmental exposure (gavage) to 1525 mg/kg bw/day of 2-ethyl-1-hexanol in pregnant mice (GD 6 to 13) caused a decrease in maternal body weight gain, reduced number of viable pups and low pup weight (Hardin 1987).

In another developmental study, dermal (occluded) exposure to 0, 252, 840, or 2520 mg/kg bw/day of undiluted 2-ethyl-1-hexanol in pregnant rats for 6 hours/day on GD 6 to 15 did not cause mortality at any dose. The only significant effect was reported to be a decrease in body weight gain in dams in the highest dose group. No gestational effects, malformations or teratogenic effects were seen at any dose (Tyl et al. 1992). Similarly, inhalation exposure to 850 mg/m^3 of 2-ethyl-1-hexanol throughout gestation (7 hours/day) did not cause any fetal malformation (Nelson et al. 1988).

9.6.3 Characterization of risk to human health

Using 100% dermal absorption, the short-term systemic exposure to 2-ethyl-1-hexanol from the use of engine cleaners was determined to be 0.12 mg/kg bw/day. From a 90-day gavage study on rats, a NOAEL of 125 mg/kg bw/day was determined for decreases in serum enzyme levels. This gives an MOE of 1025 for this exposure. This MOE is considered adequate to address uncertainties in the health effects and exposure databases.

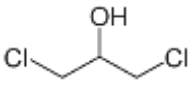
10. 1,3-Dichloro-2-propanol

10.1 Substance identity

1,3-Dichloro-2-propanol (1,3-DCP) is an anthropogenic compound not found in nature. Information regarding the substance identity of 1-3 DCP is summarized in Table 10-1 (ChemID 2017).

1,3-DCP is a member of the broad chemical class of halohydrins, which encompasses halogenated alcohols. Specifically, 1,3-DCP is a glycerol chlorohydrin, a subset of the halohydrins group in which one or two of the hydroxyl groups of glycerol (1,2,3-trihydroxypropane) have been replaced by one or two chlorine atoms.

Table 10-1. Substance identity of 1,3-DCP

CAS RN	DSL name (common name)	Molecular formula	Chemical structure	Molecular weight (g/mol)
96-23-1	2-Propanol, 1,3-dichloro- (1,3-DCP; 1,3-dichloro-2-propanol)	$C_3H_6OCl_2$		128.99

10.2 Physical and chemical properties

The physical and chemical properties of 1,3-DCP are given in Table 10-2 (PubChem 2004-). Additional physical and chemical properties data are presented in ECCC (2016b).

Table 10-2. Physical and chemical properties of 1,3-DCP (PubChem 2004-)

Property	Value

Melting point (°C)	-4
Boiling point (°C)	174
Relative density (g/cm^3)	1.39
Vapour pressure (mmHg at 25ºC)	0.75
Water solubility (g/L)	110
log K_{ow} (dimensionless)	0.78
pK_a (dimensionless)	12.87 ± 0.2

1,3-DCP is a colourless liquid with an ether-like odour and a relatively low vapour pressure. It is soluble in water.

10.3 Sources and uses

1,3-DCP is not found in nature and all occurrences are of anthropogenic origin (NTP 2005). A number of industrial and laboratory-scale synthetic routes are reported for 1,3-DCP production. However, the most common method uses the reaction of allyl chloride and hypochlorous acid. The process yields a mixture of 2,3-dichloro-2-propanol (2,3-DCP) and 1,3-DCP at a ratio of approximately 7:3 (EPA 1984).

Through a base-catalyzed process, 2,3-DCP and 1,3-DCP are reacted further to form epichlorohydrin (EPA 1984). Due to the use of epichlorohydrin, unintentional 1,3-DCP contamination can occur from thermal degradation, metabolism or leaching of unreacted components of resins or chemicals synthesized with epichlorohydrin.

Small quantities of high-purity 1,3-DCP are used for specialty applications, such as determination of vitamin A analyte (NTP 2005). The 1,3-DCP used for this purpose is not available to the general population.

According to information submitted in response to a CEPA section 71 survey 1,3-DCP was manufactured in Canada in quantities under 100 kg and imported into Canada in quantities of approximately 160 000 kg in 2011 (Environment Canada 2013).[8] In 2008, the substance was reported to be used by several companies in paper production and by one company in water treatment (Environment Canada 2009). These uses are either site- or industry-restricted and are not expected to lead to releases of 1,3-DCP to the environment during production of this substance.

1,3-DCP is not an ingredient in products available to consumers in Canada. Tris(1,3-dichloroisopropyl)phosphate (TDCPP) , a 3:1 ester of 1,3-DCP with phosphoric acid, is produced from a reaction involving epichlorohydrin. TDCPP is a flame retardant commonly added to flexible polyurethane foam in upholstery and couch cushions. TDCPP can be present in a variety of products available to consumers, including

[8] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

automobiles, upholstered furniture, camping tents, baby products and home insulation material (ECCC, HC 2016). TDCPP is an additive flame retardant, meaning that it is not chemically bonded to treated materials and is therefore more likely to be released into the surrounding environment during the lifetime of the product. 1,3-DCP has been detected in chamber test emissions from carpets and cushions indicating that degradation of TDCPP to 1,3-DCP may occur (ECCC, HC 2016).

1,3-DCP has also been identified to result from the degradation of epichlorohydrin polyamine polyelectrolytes, a series of chemicals used in water treatment (IARC 2013). In Austria, sampling from 32 river sites showed the presence of 1,3-DCP in the water but below the quantification limit. Similar findings have been made at various sites in the United States and United Kingdom (Schuhmacher et al. 2005).

Epichlorohydrin-based materials were used extensively in the past in the pulp and paper industry. As components of resins, they were employed to increase the wet strength and to bleach paper products, although the industry has made a considerable effort to reduce the concentration of chloropropanols in their resin formulations. 1,3-DCP has been found in effluents, spent bleaching liquors and municipal waste landfill leachate (IARC 2013).

Hydrolyzed vegetable proteins (HVPs) are commonly used as food flavouring agents added to processed foods. The acid-hydrolyzed manufacturing process, commonly used to produce HVP, can also unintentionally synthesize 1,3-DCP (NTP 2005; Dolan et al. 2010).

1,3-DCP is manufactured as an intermediate for epichlorohydrin production, which is then further purposed into various epoxy resins. 1,3-DCP has also historically been used in the production of several other industrially important organic compounds. Dehydration of 1,3-DCP with phosphoryl chloride forms 1,3-dichloropropene, a soil fumigant. Chlorination of 1,3-DCP with phosphorus pentachloride gives 1,2,3-trichloropropane, an industrial intermediate and solvent. Hydrolysis of dichlorohydrins has been used in the production of synthetic glycerol. These applications have been phased out in favour of safer synthetic routes to making glycerol due to the toxicity of 1,3-DCP (NTP 2005).

1,3-DCP has also been used as a solvent for hard resins and nitrocellulose, in the manufacture of photographic and Zapon lacquer, as a cement for celluloid and as a binder for watercolours (Merck Index 2017). A US patent and patent application survey shows a historic use of the chemical as a dye fixative/anti-fading agent. These applications have similarly been abandoned as a result of toxicity concerns (NTP 2005).

Various international jurisdictions, including New Zealand (New Zealand EPA 2010), the EU (CosIng 2016), and Southeast Asia (ASEAN 2018), have all prohibited the use of 1,3-DCP in cosmetics in order to prevent direct use of the chemical as a filler or colour binder and to prevent leaching from product packaging. The Cosmetic Ingredient Hotlist does not include 1,3-DCP, which is not notified in any cosmetic products in Canada, but

does describe epichlorohydrin, which may be contaminated with 1,3-DCP, as a prohibited ingredient (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2016; unreferenced).

Several other specialty uses for the substance remain. For example, it can be employed in the analytical determination of vitamin A (NTP 2005). The niche uses of the substance have not been deemed relevant for this report as they are limited to controlled settings and involve only small amounts of the substance. A survey of products available to consumers in Canada did not identify any products with 1,3-DCP (Environment Canada 2012). Applications of this substance in Canada have been reported, including use as a sizing agent in the manufacture of paper and cardboard that may be used for food packaging materials with no direct contact with food; exposure is therefore negligible (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated December, 2016; unreferenced). 1,3-DCP is not notified in any cosmetic products in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated November 17, 2016; unreferenced).

1,3-DCP is not listed in the NHPID and does not appear in any licensed NHPs in Canada (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 26, 2016; unreferenced).

10.4 Environmental fate and behaviour

10.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), 1,3-DCP is expected to persist in air, but it is not expected to persist in water, soil, or sediment.

10.4.2 Potential for bioaccumulation

Given its low log K_{ow} and low bioconcentration factor (ECCC 2016b), 1,3-DCP is not expected to significantly bioaccumulate in organisms.

10.5 Potential to cause ecological harm

10.5.1 Characterization of ecological risk

The ecological risk of 1,3-DCP has been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in the ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for 1,3-DCP, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

1,3-DCP was classified as having a moderate hazard potential according to information considered under ERC due to a reactive mode of action and structural alerts from the OECD toolbox (LMC 2017) identifying this substance as having the potential to bind to protein and DNA. However, 1,3-DCP was classified as having low exposure potential and therefore an overall low potential for ecological risk. It is therefore unlikely that this substance is resulting in concerns for the environment in Canada.

10.6 Potential to cause harm to human health

10.6.1 Exposure assessment

10.6.1.1 Environmental media and food

Exposure to 1,3-DCP from the direct addition of this substance to products available to consumers is not expected. All environmental media exposure of the substance are expected to result from unintentional formation or from the degradation/leaching/evaporation by-products of substances containing or derived from epichlorohydrin.

Epichlorohydrin polyamine polyelectrolytes are used for chemical treatment of drinking water. They are coagulation and flocculent promoters whose degradation has been associated with the formation of dichloropropanol contaminants (NTP 2005). Between 1991 and 1999, NSF International identified nine cases where 1,3-DCP and 1,2-DCP concentration exceeded the 9 ppb permissible level at that time, in products tested to NSF/ANSI Standard 60 (NSF 2000). The requirement (i.e., permissible level) as listed under NSF/ANSI/CAN Standard 60 is currently 4 µg/L for the total of 1,3-DCP and 2,3-DCP (NSF 2017). Since there is widespread adoption of NSF/ANSI/CAN Standard 60 and NSF/ANSI/CAN Standard 61 by water treatment systems in Canada (NSF 2018), exposure to 1,3-DCP from drinking water is expected to be low and well within acceptable limits where drinking water is treated with epichlorohydrin.

Additional water contamination can occur from the pulp and paper industry (NTP 2005). The process has historically utilized epichlorohydrin-based wet-strength resins to strengthen and bleach paper products. The industry has made a deliberate effort to minimize chloropropanol use in production. However, various studies have found 1,3-DCP in effluents and spent bleaching liquors from paper mill sites (IARC 2013).

The predominant source of 1,3-DCP exposure for the general population is likely from foods. Although 1,3-DCP may be used as a component in the manufacture of paper products used in food packaging materials, the exposure potential from this source, if any, has been considered negligible. 1,3-DCP is a food contaminant that can be formed during the processing of different foodstuffs. Health Canada has not established a

maximum level (ML) for 1,3-DCP, but has established an ML of 1 mg/kg 3-monochloropropane-1,2-diol (3-MCPD) in Asian-style sauces, such as soy, oyster and mushroom sauces; it is included in the *List of Maximum Levels for Various Chemical Contaminants in Food*. Since 1,3-DCP generally occurs together with 3-MCPD, which is regarded as the most abundant chloropropanol found in foods, the ML for 3-MCPD would be expected to also reduce the levels of 1,3-DCP in foods (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 2016; unreferenced). The unintended presence of 1,3-DCP in foods has been the major area of international concern and has prompted various restrictions determining permissible limits of chloropropanols in foods, a summary of which can be found in Appendix D. Prior to international regulations, varying levels of 1,3-DCP, usually averaging below 0.1 mg/kg dry weight, had been found in many foods. 1,3-DCP occurs most abundantly in soy sauce and soy sauce-based products. The concentrations in some foods, predominantly soy sauce and soy-based products, had been found to be as high as 9.84 mg/kg (JECFA 2007a; IARC 2013).

1,3-DCP may be formed in certain food processing conditions. HVPs are amino acid residues extracted from high-protein grains/seeds and added to enhance foods (CAC 2008). HVP that is made through an acid-hydrolyzed process (as opposed to enzymatically produced HVP) may produce 1,3-DCP as a by-product contaminant. The process involves heating the protein source in the presence of hydrochloric acid, which causes chlorination of residual lipids, leading to formation of chloropropanols from glycerol of the triglyceride present in the grain (CAC 2008).

Acid HVPs are commonly added to processed foods, thereby unintentionally transferring 1,3-DCP into the product. Soy sauces and soy-based products in particular have been found to contain elevated concentrations of 1,3-DCP (NTP 2005, Kim et al. 2015).

1,3-DCP has also been found in cured meats, but is suspected to be formed from the reaction of sodium chloride with fats or to have migrated into the food from resins used in sausage casings (NTP 2005).

Levels of 1,3-DCP found in foods (IARC 2013), before American, European, and Oceanic intervention to reduce occurrence, are summarized in Table 10-3.

Table 10-3. Weighted concentration distributions of 1,3-DCP in foods and food ingredients from various countries (between 2001–2006) (IARC 2013) prior to interventions to reduce this substance by government or industry

Product type	LoQ (mg/kg)	Number of products sampled	Products with concentration less than LoQ	Mean[a] (mg/kg)	Maximum (mg/kg)
Soy sauce and soy sauce–based products	0.002–0.15	484	371	0.110	9.84

Meat and meat products	0.005	99	51	0.019	0.11
Fish and seafood	0.005	29	26	0.0025	0.024
Food ingredients (including HVPs and malt extracts)	0.010	56	13	0.008	0.070

[a] Products with concentration below the limit of detection (LoD) or limit of quantification (LoQ) are assumed to be half of those limits and the mean was weighted according to the number of samples per country.

Based on information submitted to JECFA, a dietary intake of 1,3-DCP was calculated for 10 countries (Australia, Denmark, Finland, France, Germany, Ireland, the Netherlands, Sweden, Thailand and the UK) (JECFA 2007a). The highest exposures were in Australia and the UK and exposures were highest among children. Meat products were the main contributor to intake in all national estimates, ranging from 45% to 99% depending on the country diet. Soy sauce and soy sauce-based products contributed up to 30% in all national estimates, and other food groups contributed up to 10% of the total intake. JECFA also conducted a refined assessment using food consumption data for cluster diets. The global mean intake from all sources was determined to range from 0.008 µg/kg bw/day to 0.090 µg/kg bw/day (based a body weight of 60 kg). Meat products were also the main contributor to intake in most cluster diets, ranging from 54% to 72%; soy sauce and soy-based products contributed more than 10% of the total intake. Across all age groups, 95th percentile consumer exposure values range from 0.025 µg/kg bw/day to 0.136 µg/kg bw/day, with an average exposure of 0.051 µg/kg bw/day. JECFA notes that the exposure assessment "is likely to result in an overestimation of dietary exposure, but assumes a worst-case scenario" (JECFA 2007a).

10.6.1.2 Exposure from products available to consumers

Exposure from Flame Retardants

Inhalation and dermal exposures to 1,3-DCP has been estimated. Additional exposure of the general population to 1,3-DCP may potentially occur from the degradation of the flame retardant TDCPP, a 3:1 ester of 1,3-DCP and phosphoric acid (NTP 2005; ECCC, HC 2016).

Available literature data indicate that TDCPP does not hydrolyze readily at pH values between 6 and 9 and temperatures between 2 °C and 25 °C to give 1,3-DCP. Furthermore, the EU quotes a study that shows that of the metabolites of TDCPP in rat urine, no 1,3-DCP is recovered. TDCPP is considered to be completely metabolized to CO_2 (EC 2008). The metabolites of TDCPP generated by the microsomal fraction of the liver homogenate included up to 6% 1,3-DCP. However, this fraction decreased further as the nicotinamide adenine dinucleotide phosphate cofactor concentration in the solution was increased, indicating that 1,3-DCP is possibly subject to further metabolism (EC 2008).

Several studies of the TDCPP degradation pathways indicate either a quantitative detection of 1,3-DCP (in VOC emissions from carpet cushions) or a qualitative measurement (0.01 mg/m^3 to 0.1 mg/m^3 from carpet backing) in chamber test emissions (NTP 2005).

The exposure to TDCPP from environmental media and food was estimated to be 0.35 µg/kg bw/day for infants (ECCC, HC 2016). Using a conservative assumption of 10% metabolic degradation of TDCPP into 1,3-DCP based on the rat liver metabolite study, a maximum systemic exposure of 0.0314 µg/kg bw/day from this source was calculated.

The assessment of TDCPP estimated highest daily dermal exposures from contact with mattresses of 1.9 µg/kg bw/day for 0- to 0.5-year-old infants (ECCC, HC 2016). Using a conservative assumption of 100% dermal adsorption of the TDCPP and 10% degradation into 1,3-DCP based on the rat liver metabolite study, a maximum systemic exposure of 0.19 µg/kg bw/day of 1,3-DCP from this source was calculated.

In the assessment of TDCPP, the lifetime average daily dose (LADD) for TDCPP was calculated to be 0.59 µg/kg bw/day. Using the 10% metabolic degradation rate gives a general population exposure to 1,3-DCP of 0.059 µg/kg bw/day.

10.6.2 Health effects assessment

1,3-DCP has been reviewed internationally (JECFA 2007, 2006; NTP 2005). Carcinogenicity has been considered the critical effect for 1,3-DCP. The IARC classified 1,3-DCP as a Group 2B carcinogen (IARC 2013).

In a carcinogenicity study, rats were given 1,3-DCP in drinking water at 0, 2.1, 6.3, or 19 mg/kg bw/day in males and 0, 3.4, 9.6, or 30 mg/kg bw/day in females for 104 weeks. The authors reported a dose-related increase in development of hepatocellular carcinoma/adenoma, renal tubular adenoma, adenoma or carcinoma of tongue, and thyroid follicular cell carcinoma in both sexes in the two highest tested doses (RCC 1986; Williams et al. 2010). JECFA considered the RCC (1986) study to be critical and calculated the range of values of the 95% lower confidence limit of the benchmark dose ($BMDL_{10}$) to be from 7.2 to 19.1 mg/kg bw/day in male rats and from 3.3 mg/kg bw/day to 7.7 mg/kg bw/day in female rats based on incidence of tumours (JECFA 2007a).

The IARC also considered the RCC (1986) study important and concluded that 1,3-DCP is possibly carcinogenic to humans based on sufficient evidence of cancer in experimental animals (IARC 2013). JECFA (2002) acknowledged these findings and, in addition, reported a subchronic (13-week) study in which male and female rats were administered 0, 0.1, 1, 10, or 100 mg/kg bw/day of 1,3-DCP in distilled water (5 days/week) via gavage. In this study, the authors reported decreased body weight, alterations in biochemical endpoints and histopathological changes in the liver, kidney and stomach (Jersey et al. 1991). The genotoxicity potential of 1,3-DCP is not clear *in vivo*,but studies conducted *in vitro* demonstrated that 1,3-DCP can interact with

chromosomal material and influence DNA repair. Therefore, this substance may be expected to be genotoxic *in vivo* (JECFA 2002).

No carcinogenicity data were available in humans (IARC 2013). The European Commission's consolidated list of carcinogenic, mutagenic or toxic to reproduction substances includes 1,3-DCP in Carcinogens Category 2 (EC 2002).

The Committee on Carcinogenicity of Chemicals in Food of the UK Department of Health established a NOAEL of 1 mg/kg bw/day based on an increase in liver and kidney weight following subchronic (13 weeks; 5 days/week, gavage in distilled water) exposure to 0.1, 1, 10, or 100 mg/kg bw/day of 1,3-DCP in male and female rats. However, the histopathological changes in the liver, stomach and kidney were seen only in male rats (Jersey et al. 1991 cited in NTP 2005; Katoh et al. 1998). In another subchronic study, inhalation exposure to 26, 105, or 422 mg/m^3 of 1,3-DCP caused changes in hematological parameters and an increase in liver and kidney weight in the highest dose groups. The NOAEL and LOAEL were identified as < 26 mg/m^3 and 26 mg/m^3, respectively (Kim et al. 2007).

10.6.3 Characterization of risk to human health

The World Health Organization (WHO) used dose-response models and estimated the benchmark dose (BMD_{10}) and the $BMDL_{10}$ of a 10% response above background for the incidence of tumours. They ranged from 5.4 to 7.5 mg/kg bw/day and from 3.3 to 6.1 mg/kg bw/day, respectively, in male rats, and from 7.6 to 10.3 mg/kg bw/day and from 6.6 to 7.7 mg/kg bw/day, respectively, in female rats (JECFA 2007a,b).

Cancer

Comparison of the lowest $BMDL_{10}$ of 3.3 mg/kg bw/day reported for incidence data on tumour-bearing animals, with JECFA's 95th percentile mean and high end dietary exposures of 0.051 µg/kg bw/day and 0.136 µg/kg bw/day (JECFA 2007a) indicates oral MOEs of approximately 65 000 and 24 000, respectively. The required NSF/ANSI Standard 60 concentration for 1,3-DCP in drinking water of 4 µg/L using a 2 L/day consumption rate gives a MOE of 30 000. These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

A very conservative assumption of the LADD for exposure to 1,3-DCP from the decomposition of the flame retardant TDCPP estimates a general population exposure of 0.059 µg/kg bw/day. Compared with the $BMDL_{10}$ of 3.3 mg/kg bw/day gives an MOE for this exposure of 56 000. This MOE is considered adequate to address uncertainties in the health effects and exposure databases.

Non-cancer

Using the NOAEL of 1 mg/kg bw/day for the non-cancer endpoint of increased kidney and liver weights, the oral exposure of 0.136 µg/kg bw/day via food consumption estimated by JECFA (JECFA 2007a) gives an MOE of 7300. This MOE is considered adequate to address uncertainties in the health effects and exposure databases.

Considering the combined food and environmental media exposures to 1,3-DCP from TDCPP metabolic degradation, a total exposure of 0.136 + 0.03 = 0.166 µg/kg bw/day is obtained. This gives an MOE of 6000, which is considered adequate to address uncertainties in the health effects and exposure databases. Considering the dermal exposure from TDCPP metabolic degradation in mattresses, the total systemic exposure becomes 0.19 µg/kg bw/day. This gives an MOE of 5300, which is considered adequate to address uncertainties in the health effects and exposure databases.

While exposure of the general population to 1,3-DCP is not of concern at current levels, this substance is considered to have a health effect of concern on the basis of its potential IARC Group 2B carcinogen designation. Therefore, there may be a concern for human health if exposures were to increase. Options are being considered for follow-up activities to track possible changes in exposure to 1,3-DCP.

10.7 Uncertainties in evaluation of risk to human health

There is uncertainty in the daily amount of foods consumed that contain residual 1,3-DCP. The values of the 1,3-DCP exposure from different food groups used in this assessment were determined by JECFA from the survey of a limited number of countries.

11. 2-Propen-1-ol

11.1 Substance identity

Information regarding the identity of 2-propen-1-ol (allyl alcohol) is summarized in Table 11-1 (PubChem 2004-).

Table 11-1. Substance identity of allyl alcohol

CAS RN	DSL name (common name)	Molecular formula	Chemical structure	Molecular weight (g/mol)
107-18-6	2-Propen-1-ol (allyl alcohol)	C_3H_6O		58.08

11.2 Physical and chemical properties

Measured values for the physical and chemical properties of allyl alcohol are given in Table 11-2 (ChemIDplus 2017). Additional physical and chemical properties are presented in ECCC (2016b).

Table 11-2. Physical and chemical properties of allyl alcohol

Melting point (°C)	Boiling point (°C)	log K_{ow} (dimensionless)	Water solubility (mg/L)	Vapour pressure (mm Hg)
–129	97	0.17	6.32×10^4	26.1

11.3 Sources and uses

Allyl alcohol is an industrially significant chemical and is manufactured worldwide. According to information submitted in response to a CEPA section 71 survey, the substance was not manufactured in Canada in 2011, but 7700 kg were imported into Canada that year (Environment Canada 2013).[9]

Allyl alcohol is used in Canada in industrial paints and coatings as a copolymer reactant, as a corrosion inhibitor, as a deposit control product, as a laboratory substance, and as raw material for high-tech manufacturing (Environment Canada 2013). The anthropogenic manufacturing of allyl alcohol is through the hydrolysis of allyl chloride. It is also found naturally in crab meat, rotten mussels, and in crushed garlic as a volatile component. In garlic, allyl alcohol is a metabolic product formed during the trituration of garlic cloves (Lemar 2005). Allyl alcohol is also formed in the body from the hydrolysis of allyl esters used as food flavouring agents (OECD 2004e).

Allyl alcohol may be used as a component in the manufacture of paper and paperboard food packaging materials, with the potential for direct food contact and exposure (personal communication, email from the Food Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 2016; unreferenced). Allyl alcohol is not notified in cosmetics in Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 2016; unreferenced). Allyl alcohol is not listed in the NHPID and does not appear in any licensed NHPs in Canada (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada, to the Risk Management Bureau, Health Canada, dated October 26, 2016; unreferenced).

11.4 Environmental fate and behaviour

11.4.1 Environmental persistence

According to models used in ERC (ECCC 2016b), allyl alcohol is not expected to persist in air, water, soil, or sediment.

11.4.2 Potential for bioaccumulation

Given its low log K_{ow} and low bioconcentration factor (ECCC 2016b), allyl alcohol is not expected to significantly bioaccumulate in organisms.

[9] Values reflect quantities submitted in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

11.5 Potential to cause ecological harm

11.5.1 Characterization of ecological risk

The ecological risk of allyl alcohol has been characterized using the ERC approach. The approach is summarized in Appendix A, and the results of its application are presented in ECCC (2016a).

Critical data and considerations used to develop the substance-specific profile for allyl alcohol, as well as the hazard, exposure and risk classification results, are presented in ECCC (2016b).

On the basis of low hazard and low exposure classifications according to information considered under ERC, allyl alcohol was classified as having a low potential for ecological risk. It is therefore unlikely that this substance is resulting in concerns for the environment in Canada.

11.6 Potential to cause harm to human health

11.6.1 Exposure assessment

There are no products available to consumers that contain allyl alcohol. For that reason, direct exposures are not considered.

11.6.1.1 Environmental media and food

The main industrial use of allyl alcohol is as a reactive copolymer in paints and coatings. Most of the substance is expect to react in forming the resulting polymers. There may be limited releases to the environment from its industrial uses.

There is a potential for allyl alcohol to be present in water and air in limited quantities. Based on calculated results from a level III fugacity model, allyl alcohol is expected to partition primarily to air (67.6%) and water (25.1%), with the remainder to soil (7.3%) (OECD 2005b). It has been shown to biodegrade rapidly in aerobic, aqueous biodegradation tests and therefore is not expected to persist in aquatic environments. It is also not expected to remain in surface soils due to rapid evaporation to the air. Any releases of allyl alcohol to the atmosphere through various use streams will result in vapour-phase allyl alcohol being degraded by reaction with photochemically produced hydroxyl radicals (half-life 15 hours) (Atkinson et al. 1989), by reaction with ozone (half-life of 19 hours) (Atkinson and Carter 1984), or by nitrate radicals (half-life of 31 hours) at night (Atkinson 2000). As a result, significant exposure of the general population from this route is not expected.

This is supported by a study performed by the Japanese Ministry of Environment in 2004, which found the average total human exposure to allyl alcohol from environmental air, well water, and public water to be less than the minimum detection limit (OECD 2005b). From this study, the OECD determined that the total oral exposure from well

water or public water was 0.012 µg/kg bw/day, and the total inhalation exposure from environmental air was estimated to be 0.015 µg/kg bw/day.

Allyl alcohol occurs naturally in certain foods, namely crab, rotten mussels, and garlic (OECD 2005b). Allyl alcohol was detected at concentrations of 0.3 µg/kg dry weight in the legs and claws and 0.1 µg/kg dry weight in the body meat of crabs (Chung 1999). It was found at concentrations of 1,080 µg/kg wet weight in rotten mussels (Yasuhara 1987). Allyl alcohol concentration was measured from six samples of crushed garlic bulbs to give a median (average) value of 29.6 (43.7) mg/kg. The concentration of allyl alcohol in garlic was affected by the method used to remove the garlic oils from the water phase (Yu et al. 1989). The method of extraction is important since allyl alcohol is produced from enzyme activity, which may be affected by the extraction method. Allyl alcohol is released after the ingestion of garlic (Egen-Schwind et al. 1992) and has been detected in exhaled air after ingestion of all garlic products (Laasko 1989).

Allyl alcohol may also form in the body by hydrolysis of allyl esters found as flavouring agents in food. The estimated intake of allyl alcohol from crab meat and garlic is 18 µg/kg bw/day in Europe and 5.8 µg/kg bw/day in the United States (OECD 2005b).

Oral exposure to allyl alcohol found in crab and garlic is assumed to represent the greatest source of exposure. Table 12-3 gives the amount of allyl alcohol found in crab meat and garlic, average daily consumption values for these food items, and daily oral exposure calculations from available data. These exposures consider the conservative assumptions that three servings (75 g/serving) of crab and four cloves (3 g/clove) of garlic are eaten per day.

Table 11-3. Daily oral exposures to allyl alcohol from crab meat and garlic

Food type	Concentration of allyl alcohol	Daily consumption of food	Oral exposure (µg/kg bw/day)
Crab meat [a]	0.3 µg/kg dry weight	225 g	0.001 [b]
Garlic [c]	29.6 mg/kg	4 × 3 g	5 [b]

[a] Calculated from Canada's Food Guide (Health Canada 2011). The recommended number of "meat and alternative" servings per day for adults (19 to 50 years) is 2 to 3 servings. One of these serving groups is "cooked fish, shellfish, poultry, lean meat," recommended at 75 g/serving.
[b] Calculated by multiplying the acute consumption amount by concentration of allyl alcohol, then dividing by 70 kg (average adult body weight).
[c] Calculated using the University of Maryland Medical Center's recommended number of 4 cloves of garlic per day as a health supplement and possible high consumption limit and given the average "wet" weight of a clove of 3 g.

11.6.2 Health effects assessment

Allyl alcohol has been reviewed internationally for human health. A toxicological assessment was prepared in 2005 by the OECD as part of its Screening Information Data Set (OECD 2005b). Another review was published by the US EPA Integrated Risk Information System (US EPA 1987). The ECHA published a registration dossier for allyl alcohol in 2016. These documents, as well as assessments prepared by other jurisdictions, were used to inform the hazard information presented herein.

In a 13-week study, allyl alcohol was administered via drinking water at 0, 0.13, 0.62, 5.9, 11.6, 25.5, 41, or 72 mg/kg bw/day to male rats and 0, 0.17, 0.94, 7.3, 13.2, 34, 43.7, or 67.4 mg/kg bw/day to female rats. Water intake decreased in a dose-dependent manner indicating a palatability issue. A decrease in body weight gain was seen in both sexes in the two highest dose groups. An increase in kidney weight in both sexes or an increase in liver weight in male rats only was observed at 41 mg/kg bw/day or higher dose group. The NOAELs were reported as 11.6 mg/kg bw/day for males and 13.2 mg/kg bw/day for females based on increase in kidney or liver weight, which may have resulted from dehydration (Dunlap et al. 1958).

A 15-week exposure to allyl alcohol in drinking water at 0, 4.8, 8.3, 14, or 48.2 mg/kg bw/day in male rats and 0, 6.2, 6.9, 17.1, or 58.4 mg/kg bw/day in female rats caused a decrease in food intake and body weight at 14 mg/kg bw/day in males and at 58.4 mg/kg bw/day in females. A decrease in water intake was seen in animals in the highest dose group. An increase in absolute or relative kidney weight was also observed in male and female rats, especially at the highest dose. The NOAEL in this study was reported as 4.8 mg/kg bw/day in males and 6.2 mg/kg bw/day in females, and the majority of these findings were attributed by the authors as secondary to reduction in water intake, in particular, in the high-dose group (OECD 2005b; Carpanini et al. 1978).

Subchronic (12-week) inhalation exposure to allyl alcohol in male rats at 0, 2.4, 4.7, 12, 47, 95, 142, 237, or 355 mg/m^3 (7 hours/day, 5 days/week) caused no clinical signs of toxicity at 47 mg/m^3 or lower doses. However, signs of toxicity increased at higher doses and included a decrease in body weight gain and an increase in kidney or lung weight. A NOAEC of 12 mg/m^3 and a LOAEC of 47 mg/m^3 were reported in this study (Dunlap et al. 1958).

In a reproductive/developmental study, male and female rats were given allyl alcohol by gavage at 0, 2, 8, or 40 mg/kg bw/day throughout mating, pregnancy and up to day 3 of lactation. Parental animals showed salivation, decrease in locomotor activity, irregular respiration, lacrimation, loose stool and rough surface of liver at the highest dose (40 mg/kg bw/day) in males. In females, atrophy of the thymus and hyperplasia of luteal cells in the ovary were reported in the 40 mg/kg bw/day dose group. Evidence of necrosis in the liver and hypertrophy of the bile duct was also seen in both sexes in the highest dose group. No adverse effects were observed on reproductive parameters in either sex. Females showed irregular estrous cycle at the highest dose. There were no adverse effects in the offspring. The highest dose appeared to be the LOAEL for general, reproductive or developmental toxicity (Allyl Alcohol Consortium 2004b; OECD 2005b).

In a prenatal developmental study, allyl alcohol was administered by gavage at 0, 10, 35, or 50 mg/kg bw/day to pregnant rats on GD 9 to 19. Significant maternal toxicity was seen at 35 mg/kg bw/day and 50 mg/kg bw/day, including mortality, reduction in body weight gain and feed consumption, increased liver weight, and increased frequency of total litter loss. However, no increase in malformation rate or incidence of variation was

observed. Allyl alcohol was found to have no effect on intrauterine growth or survival in the fetuses from dams that survived to necropsy. A NOAEL of 10 mg/kg bw/day was reported for maternal toxicity based on liver weight and a LOAEL of 10 mg/kg bw/day was reported based on increased frequency of litter loss in the high-dose group (Lyondell Chemical Company 2005).

No clear evidence of genotoxicity potential of allyl alcohol was determined as there is equivocal evidence of mutagenicity data *in vitro* and *in vivo*. Moreover, there is no clear evidence of carcinogenicity in male rats, but there was equivocal evidence of carcinogenicity in the liver (hepatic nodules, carcinoma) of female rats given 3200 mg of allyl alcohol in drinking water for 106 weeks (OECD 2005b).

11.6.3 Characterization of risk to human health

The average daily oral exposure is for garlic at 5 µg/kg bw/day. Allyl alcohol has a LOAEL of 10 mg/kg bw/day for developmental/reproductive toxicity, primarily from observed maternal toxicity and minor paternal toxicity in rats. For this exposure, an MOE value of 2000 is determined.

The MOE is considered adequate to address uncertainties in the health effects and exposure databases.

11.7 Uncertainties in evaluation of risk to human health

There is some uncertainty surrounding the source and use of the concentration of allyl alcohol in crab meat. The live crabs were purchased from a seafood outlet in Hong Kong in 1996 and immediately steamed for 20 minutes. Due to the isolated sample, there is a possibility that allyl alcohol is present at such a concentration only at the specific site where the sample of crabs were caught or where processing of the live crabs occurred prior to purchase, thus altered their allyl alcohol exposure. In addition, the use of 75 g of crab per serving for 3 servings a day was a conservative value that is likely to be above average daily crab consumption in Canada.

12. Conclusions

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to the environment from the 21 alcohols in this screening assessment. It is proposed to conclude that the 21 alcohols in this screening assessment do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Considering all the information presented in this draft screening assessment, it is proposed to conclude that methanol, 1-butanol and benzyl alcohol meet the criteria

under paragraph 64(c) of CEPA as they are entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is also proposed to conclude that the remaining 18 alcohols in this screening assessment do not meet the criteria under paragraph 64(c) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Therefore, it is proposed to conclude that methanol, 1-butanol, and benzyl alcohol (benzenemethanol) meet one or more of the criteria set out in section 64 of CEPA and that the other 18 alcohols in this screening assessment do not meet any of the criteria set out in section 64 of CEPA.

It is also proposed that methanol meets the persistence but not the bioaccumulation criteria and that 1-butanol and benzyl alcohol (benzenemethanol) do not meet the persistence or bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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Appendix A. Description of the ecological risk classification of organic substances approach

The ecological risks of the substances in the Alcohols Group were characterized using the ERC approach (ECCC 2016a). The ERC is a risk-based approach that considers multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. The various lines of evidence are combined to discriminate between substances of lower or higher potency and lower or higher potential for exposure in various media. This approach reduces the overall uncertainty with risk characterization compared to an approach that relies on a single metric in a single medium (e.g., median lethal concentration) for characterization. For UVCB substances that could not be suitably represented by a single chemical structure, a manual judgment-based approach to classification was used. The following summarizes the approach, which is described in detail in ECCC (2016a).

Data on physical-chemical properties, fate (chemical half-lives in various media and biota, partition coefficients, fish bioconcentration), acute fish ecotoxicity, and chemical import or manufacture volume in Canada were collected from scientific literature, from available empirical databases (e.g., OECD QSAR Toolbox 2014), from responses to surveys under CEPA section 71, or were generated using selected (quantitative) structure-activity relationship ([Q]SAR) or mass-balance fate and bioaccumulation models. These data were used as inputs to other mass-balance models or to complete the substance hazard and exposure profiles.

Hazard profiles were based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Exposure profiles were based on multiple metrics, including potential emission rate, overall persistence, and long-range transport potential. Hazard and exposure profiles were compared to decision criteria in order to classify the hazard and exposure potentials for each organic substance as low, moderate, or high. Additional rules were applied (e.g., classification consistency, margin of exposure) to refine the preliminary classifications of hazard or exposure. However, in the case of some UVCBs, hazard and exposure could not be fully profiled because of the lack of a representative structure to estimate needed properties and the lack of empirical data for these properties. Therefore, manual classification of hazard and exposure was performed by examining the UVCB constituents and information submitted in response to a CEPA section 71 survey, making decisions on the basis of consideration of similar substances and application of expert judgment.

A risk matrix was used to assign a low, moderate, or high classification of potential risk for each substance on the basis of its hazard and exposure classifications. ERC classifications of potential risk were verified using a two-step approach. The first step adjusted the risk classification outcomes from moderate or high to low for substances that had a low estimated rate of emission to water after wastewater treatment, representing a low potential for exposure. The second step reviewed low risk potential classification outcomes using relatively conservative, local-scale (i.e., in the area

immediately surrounding a point source of discharge) risk scenarios, designed to be protective of the environment, to determine whether the classification of potential risk should be increased.

ERC uses a weighted approach to minimize the potential for both over- and under-classification of hazard, exposure, and of subsequent risk. The balanced approaches for dealing with uncertainties are described in greater detail in ECCC (2016a). The following describes two of the more substantial areas of uncertainty. Error in empirical or modelled acute toxicity values could result in changes in classification of hazard, particularly metrics relying on tissue residue values (i.e., mode of toxic action), many of which are predicted values from (Q)SAR models (OECD QSAR Toolbox 2014). However, the impact of this error is mitigated by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue value used for critical body residue analysis. Error in underestimation of acute toxicity will be mitigated through the use of other hazard metrics such as structural profiling of mode of action, reactivity and/or estrogen-binding affinity. Changes or errors in chemical quantity could result in differences in classification of exposure as the exposure and risk classifications are highly sensitive to emission rate and use quantity. The ERC classifications thus reflect exposure and risk in Canada on the basis of what is estimated to be the current use quantity and may not reflect future trends.

Appendix B. Exposure factors for general population exposures to products containing methanol, 1-butanol, cyclohexanol, and benzyl alcohol

Table B-1. Input variables for dispersion modelling for inhalation exposure to methanol near an industrial facility using SCREEN3

Variable	Input Variable
Source type	Area
Effective emission area[a]	600 × 600 m^2
Emission rate	25.75 (g/s)
Receptor height[b]	1.74 m (average adult height)
Source release height[a]	10 m
Adjustment factor[c]	0.4 (variable wind direction during 24-hour period); 0.2 (average wind direction during 1-year period)
Urban–rural option	Rural
Meteorology[d]	1 (full meteorology)
Minimum and maximum distance	0–2000 m

[a] Professional judgment.
[b] Curry et al. (1993).
[c] US EPA (1992).
[d] Default value in SCREEN3.

Table B-2. Ambient air concentrations of methanol in the vicinity of an industrial release area

Distance (m)	Maximum 1-hour concentration of methanol (µg/m^3)	Maximum annual concentration of methanol (µg/m^3)
1	973.5	194.7
100	1241	248.2
200	1485	297.0
300	1777	355.4
400	2046	409.2
500	2296	459.2
600	2452	490.4
700	2603	520.6
800	2629	525.8
900	2586	517.2
1000	2512	502.4
1100	2427	485.4
1200	2340	468.0
1300	2256	451.2
1400	2175	435.0

1500	2099	419.8
1600	2027	405.4
1700	1959	391.8
1800	1896	379.2
1900	1837	367.4
2000	1782	356.4

Table B-3. Input variables and calculated concentrations (mg/m^3) for inhalation exposure to methanol from paint and varnish remover use (ConsExpo Exposure to Vapour model –evaporation mode)

Variable	**Input variable**		
Exposure scenario	Paint and varnish remover		
Size of project	Small project	Large project	Bathtub resurfacing
Amount of product used	500 g	4500 g	1650 g
Product release area	1 m^2	9 m^2	3.3 m^2
Methanol emission factor	50 %	50 %	50 %
Application duration	20 min	20 min	20 min
Exposure duration	90 min	90 min	90 min
Volume of room	34 m^3	34 m^3	~~3~~410 m^3
Ventilation rate	0.5 to 2.5 hr^{-1}	0.5 to 2.5 hr^{-1}	2.0 hr^{-1}
Cap to limit concentration to saturated vapour	12.8 kPa	12.8 kPa	12.8 kPa
5% methanol -Mean event concentration -Peak concentration -Mean concentration on day of exposure	 215[a] – 110[b] 295[a] – 185[b] 10.5[a] – 5.0[b]	 1800[a] – 8500[b] 2400[a] – 1550[b] 90[a] – 46[b]	 1350 2100 65
35% methanol -Mean event concentration -Peak concentration -Mean concentration on day of exposure	 1500[a] – 760[b] 2050[a] – 1300[b] 72[a] – 37[b]	 13 000[a] - 6600[b] 17 000[a] – 11 000[b] 610[a] – 320[b]	 9400 15 000 460

[a] For ventilation rate of 0.5 hour^{-1}.
[b] For ventilation rate of 2.5 hour^{-1}.

Table B-4. Input variables for calculating inhalation exposure to methanol from all-purpose spray cleaner, hairstyling product and muscle pain relief product use in ConsExpo (RIVM 2006, 2018)

Variable	**Input variable**
Exposure scenario	**All-purpose spray cleaner: Application-Spraying**

Amount of product used (percent methanol)	22.1 g (5%)
Exposure duration	60 min
Volume of room	58 m^3 (bathroom)
Ventilation rate	0.5 hr^{-1}
Inhalation rate	16.3 L/min
Exposure scenario	**Hairstyling product**
Amount of product used (percent methanol)	2 g (3%)
Exposure duration	10 min
Volume of room	10 m^3 (bathroom)
Ventilation rate	2 hr^{-1}
Exposure scenario	**Muscle pain relief liquid**
Amount of product used (percent methanol)	2 mL (50%)
Breathing volume for release of methanol vapour	1 m^3
Duration of inhalation	1 min
Uses per day	3

Table B-5. Input variables for calculating inhalation exposure to 1-butanol from spray paint use in ConsExpo (RIVM 2007)

Variable	Input variable
Exposure scenario	Exposure to spray
Mass generation rate	0.45 g/s
Use duration	15 min
Exposure duration	20 min
Volume of room	34 m^3
Ventilation rate	1.5 hr^{-1}
Inhalation rate[a]	16.3 m^3/day
Average adult weight	70.9 kg

[a] Health Canada 1998.

Table B-6. Input variables for calculating inhalation exposure to 1-butanol from two-part acrylic coating use in ConsExpo (RIVM 2007)

Variable	Input variable
Exposure scenario	Exposure to vapour: constant rate
Amount of product used	900 g
Exposure duration	60 min
Emission duration	24 hr
Volume of room	35 m^3
Ventilation rate	1.5 hr^{-1}
Cap to limit concentration to saturated vapour	6.7 mmHg
Inhalation rate[a]	16.3 m^3/day

Average adult weight	70.9 kg

[a] Health Canada 1998.

Table B-7. Input variables for calculating inhalation exposure to 1-butanol from lacquer/varnish use in ConsExpo (RIVM 2007)

Variable	Input variable
Exposure scenario	Lacquer scenario
Amount of product used	500 g
Exposure duration	60 min
Volume of room	50 m^3
Ventilation rate	1.5 hr^{-1}
Cap to limit concentration to saturated vapour	6.7 mmHg
Inhalation rate [a]	16.3 m^3/day
Average adult weight	70.9 kg

[a] Health Canada 1998.

Table B-8. Input variables for calculating inhalation exposure to cyclohexanol from hobby flake enamel glaze use in ConsExpo (RIVM 2007)

Variable	Input variable
Exposure scenario	'Constant rate' model
Amount of cyclohexanol in product used	0.89 g
Exposure duration	60 min
Volume of room	58 m^3
Ventilation rate	1.5 hr^{-1}

Table B-9. Input variables for calculating inhalation exposure to cyclohexanol from ceramic overglaze use in ConsExpo (RIVM 2007

Variable	Input variable
Exposure scenario	'Constant rate' model
Amount of cyclohexanol in product used	4.5 g
Exposure duration	60 min
Volume of room	58 m^3
Ventilation rate	1.5 hr^{-1}

Table B-10. Oral exposures to benzyl alcohol at the highest concentration from cosmetics, NHPs, and non-prescription drugs

Product	Frequency of use/day	Amount ingested (g)	wt%	Calculated dose (mg/kg bw/day)
Lip balm adult	2.40	0.01	3	0.010
Lip balm teen	2.40	0.01	3	0.012
Toothpaste adult	2.0	0.08	3	0.068
Toothpaste teen	2.0	0.08	3	0.081
Toothpaste child	2.0	0.14	3	0.27
Mouthwash adult	1.0	1.7	3	0.72
Mouthwash teen	1.0	1.7	3	0.86
Mouthwash child	0.85	1.0	3	0.82

[a] Exposure factors for internal Health Canada guidance documents are used.

Table B-11. Systemic exposures to benzyl alcohol from NHPs[a]

Product	Frequency of use/day	Amount used (g)	Weight%	Systemic exposure [b] (mg/kg bw/day)
Sunscreen children 2-3 years old[c]	1	3	1.74	1.7
Sunscreen adult[c]	1	12	1.74	1.4
Face cleanser adult[d]	1.60	2.6	10	0.029
Face cleanser teen[d]	0.70	2.6	10	0.015
Face cleanser child[d]	0.70	2.5	10	0.028

[a] Exposure factors for internal Health Canada guidance documents are used.
[b] For use frequency of less than 1 per day, the systemic exposure on the day of exposure was calculated.
[c] A dermal absorption factor of 0.5 are used for the benzyl alcohol in sunscreen.

[d] A retention factor of 0.01 and dermal absorption of 0.5 are used for this wash-off product.

Table B-12. Systemic exposures to benzyl alcohol from cosmetic products (dermal absorptions of 0.5 are used in the calculations)

Product	Age group	Frequency of use/day	Amount used (g)	Retention factor	Maximum weight %	Systemic exposure [a] (mg/kg bw/day)
Body cream/ moisturizer	0–5 m	0.8	2	1	10	159
	to	0.8	2.5	1		137
	19+	0.8	3.1	1		141
		0.8	4.1	1		137
		0.8	5	1		108
		0.8	7.7	1		92
		0.8	10	1		81
		1.0	10	1		68
Deodorant/ antiperspirant (roll-on)	9–13	1.1	0.4	1	20	1.0
	14–18	1.1	1	1		1.7
	19+	1.3	1	1		1.7
Eye makeup remover	4–8	0.5	0.5	0.1	1	0.011
	9–13	0.5	0.5	0.1		0.006
	14–18	1	0.5	0.1		0.002
	19+	1.2	0.5	0.1		0.002
Face cream	9–13	1	1.1	1	10	1.3
	14–18	1	1.5	1		1.2
	19+	2	1.5	1		2.0
Face makeup/ foundation	4–8	1	0.34	1	10	7.4
	9–13	1	0.39	1		4.6
	14–18	1	0.41	1		3.3
	19+	1.2	0.54	1		4.4
Fragrance	9–13	1.4	4.3	1	10	7.2
	14–18	1.4	4.3	1		4.8
	19+	1.7	4.3	1		4.9
Shampoo	0–5 m	0.64	3.9	0.01	3	0.31
	6–11m	0.64	5.6	0.01		0.31
	1 y	0.64	6.1	0.01		0.28
	2–3	0.65	7.4	0.01		0.17
	4–8	0.64	9.7	0.01		0.21
	9–13	0.7	7.5	0.01		0.09
	14–18	0.7	10.4	0.01		0.08
	19+	1.1	11.8	0.01		0.09
Massage oil	6–11m	0.13	1.8	1	1	0.99
	1 y	0.13	1.8	1		0.82
	2–3	0.13	1.8	1		0.60
	4–8	0.13	1.9	1		0.41
	9–13	0.13	2.3	1		0.27

	14–18 19+	0.11 0.11	2.9 3.2	1 1		0.23 0.22
Nail-polish remover	2–3 4–8 9–13 14–18 19+	0.05 0.13 0.13 0.2 0.18	0.76 0.76 2.25 2.25 2.25	1 1 1 1 1	3	0.76 0.5 0.8 0.54 0.46

[a] For use frequency of less than 1 per day, the systemic exposure on the day of exposure was calculated

Table B-13. Input variables for calculating dermal exposure to benzyl alcohol from grime cleaner use in ConsExpo (RIVM 2018)

Variable	Input variable
Exposure scenario	Grime cleaner
Amount of benzyl alcohol in product used	0.29 g
Frequency of use	197 per year
Dermal absorption rate	50%
Average adult weight	70.9 kg

Table B-14. Input variables for calculating inhalation exposure to benzyl alcohol from all-purpose spray cleaner use in ConsExpo (RIVM 2018)

Variable	Input variable
Exposure scenario	All-purpose spray cleaner
Amount of product used	16.7 g
Application time	20 min
Exposure duration	240 min
Volume of room	58 m^3
Ventilation rate	0.5 hr^{-1}
Cap to limit concentration to saturated vapour	0.94 mmHg
Inhalation rate[a]	16.3 m^3/day
Average adult weight	70.9 kg

Table B-15. Input variables for calculating inhalation exposure to benzyl alcohol from liquid air freshener use in ConsExpo (RIVM 2018)

Variable	Input variable
Exposure scenario	Constant release scenario
Amount of product used / specific gravity / percent benzyl alcohol	5.5 mL / 1.02 / 5%
Exposure time	20 min
Exposure frequency	5 times per day
Duration of use of product	30 days
Volume of room	20 m^3
Ventilation rate	0.6 hr^{-1}
Cap to limit concentration to saturated vapour	0.94 mmHg
Inhalation rate[a]	9.3 m^3/day
Average adult weight	70.9 kg

Table B-16. Input variables for calculating inhalation exposure to benzyl alcohol from epoxy shield coating use in ConsExpo (RIVM 2018)

Variable	Input variable
Exposure scenario	General shield coating Exposure to vapour: Constant rate
Amount of product used	3000 g
Percent of benzyl alcohol in product	70
Exposure duration	60 min
Emission duration	24 hr
Duration of use of product	35 days
Volume of room	35 m^3
Ventilation rate	1.5 hr^{-1}
Cap to limit concentration to saturated vapour	0.094 mmHg
Inhalation rate[a]	14.4 m^3/day
Average adult weight	70.9 kg

[a] Light activity (Health Canada 1998).

Table B-17. Systemic exposures and MOEs for benzyl alcohol in cosmetic products

Product	Age group (years)	Systemic exposure (mg/kg bw/day)	MOE
Body cream/moisturizer	0–5 month	159	2.5 to 5.9
	6–11 month	137	2.9
	1	141	2.8
	2–3	137	2.9
	4–8	108	3.7
	9–13	92	4.3
	14–18	81	5.0
	19+	68	5.9
Deodorant/antiperspirant	9–13	3.3	122
	14–18	8.6	46
	19+	7.8	51
Eye makeup remover	4–8	0.011	37 000
	9–13	0.006	67 000
	14–18	0.002	220 000
	19+	0.002	260 000
Face cream	9–13	1.3	305
	14–18	1.2	330
	19+	2.0	197
Face makeup/foundation	4–8	7.4	54
	9–13	4.6	86
	14–18	3.3	121
	19+	4.4	91

Fragrance	9–13 14–18 19+	7.2 4.8 4.9	56 82 81
Hair mousse	2–3 4–8 9–13 14–18 19+	19 14 8.7 6.2 5.2	21 29 46 64 77
Hair shampoo	0–5 month 6–11 month 1 2–3 4–8 9–13 14–18 19+	0.31 0.31 0.28 0.17 0.21 0.09 0.08 0.09	1290 1300 1440 2340 1900 4480 4800 4560
Massage oil	6–11 month 1 2–3 4–8 9–13 14–18 19+	0.99 0.82 0.60 0.41 0.27 0.23 0.22	404 489 667 968 1460 1710 1850
Nail-polish remover	2–3 4–8 9–13 14–18 19+	0.76 0.5 0.8 0.54 0.46	526 807 498 735 877

Appendix C. Maximum methanol concentrations in food categories

Table C-1. Maximum methanol concentrations applied to each food category used in the dietary exposure assessment

Food category used in dietary exposure assessment	Maximum methanol concentration (ppm)	Food with the maximum concentration	Reference
Beer[a]	34	Taiwanese beer	Wang et al. 2004 DCP
Brandy[a]	9300	Pear brandy	Nosko 1974 [VCF] ‡
Fortified wine* [a]	329	Fortified wine	Rodda et al. 2013
Spirits* [a]	328	Whiskey	Rodda et al. 2013
Wine[a]	209	Red wine	Montedoro and Bertuccioli 1983 [VCF] ‡
Fruit – citrus[b]	213	Valencia orange juice	Lum et al. 1990 [VCF] ‡
Fruit – other [b]	16	Raspberries	Duclos et al. 1971 [VCF] ‡
Dairy products[b]	0.009†	Butter	Nawar et al. 1988 [VCF] ‡
Juice – apple[b]	136	Golden delicious juice	Ishii and Yokotsuka 1972
Juice – grape[b]	132	Delaware grape juice	Ishii and Yokotsuka 1973
Juice – grapefruit[b]	73.5	(Unpasteurized)	Shaw et al. 2000 [VCF] ‡
Juice – orange[b]	213	Valencia orange juice	Lum et al. 1990 [VCF] ‡
Juice – tomato [b]	560	Unpasteurized	Nelson and Hoff 1969 [VCF] ‡
Juice – other [b]	113	Pineapple juice	Hou et al. 2008
Legumes[b]	4.4	Lentils	Lovegren et al. 1979 [VCF] ‡
Tomatoes and tomato sauce[b]	430	Fresh tomato	Baldwin et al. 1991 [VCF] ‡
Vegetables[b]	0.6	Cooked cabbage	MacLeod and MacLeod 1970 [VCF] ‡
Vinegar[b]	193	Red wine vinegar	Callejón et al. 2008 [VCF] ‡

*Coolers made with vodka or fortified wine were captured under the spirits and fortified wine categories, respectively.
†Reported value was < 0.009 ppm.
‡ [VCF] = Volatile Compounds in Foods database (Nijssen et al. 1953–2017).
[a] Alcoholic beverages.
[b] Natural Sources (other than Alcoholic Beverages).

Appendix D. Summary of identified international regulations pertaining to 1,3-DCP adapted from National Toxicology Program 2005 report

Table D-1. International regulations pertaining to 1,3-DCP

Country or Organization	Judicial Body/ Act/Provision	Regulation detail
United States	Toxic Substances Control Act (TSCA)	1,3-DCP is recognized under the TSCA, which subjects producers and importers of the chemical to various restrictions, reporting, testing and record keeping requirements
United States	Food Chemicals Codex	Limits 1,3-DCP to 0.05 mg/kg (50 ppb) in soy sauce, calculated on a dry basis
United States	FDA	21CFR 173.60: Dimethylamine-epichlorohydrin copolymer (DEC) is used as a decolourizing agent or flocculating agent in the clarification of refined sugar liquids and juices. Its concentration is limited to 150 ppm of sugar solids. Concentrations of 1,3-DCP and epichlorohydrin in DEC are required to be less than 1000 ppm and 10 ppm, respectively. 21CFR173.357: This section was amended in the table in paragraph by addition of the following information: DEC may be used as a fixing material to immobilize glucose isomerase enzyme preparations. The fixed enzyme preparations are used in production of high-fructose corn syrup. The mandated residual limit of 1 000 ppm 1,3-DCP in DEC was estimated to pose minimal lifetime cancer risk to humans exposed to the impurity.
United States	EPA	Details the amount of 1,3-DCP permissible in industrial solid waste and off gas
Australia / New Zealand	Food Standards Council	Food Standards Code for soy sauce and oyster sauce: 0.005 mg/kg 1,3-DCP calculated on 40% dry weight.
New Zealand	Cosmetic Products Group Standard	Components that cosmetic products must not contain
United Kingdom	Dangerous Substance and Preparations Regulations	Schedule 2 Substance: Referred to in Regulations 6A, 6B, and 6C

United Kingdom	FSA	Advisory to the food industry to reduce 3-MCPD concentrations as low as technologically feasible
European Union	Consolidated List of C/M/R [Carcinogenic, Mutagenic or Toxic to Reproduction] Substances	Includes 1,3-DCP in the group Carcinogens, Category 2
European Union	Included on the 2000 OECD List of High Production Volume Chemicals	Co-operatively investigate.to identify those which are potentially hazardous to the environment and/or to the health of the general public or workers
European Union	European Commission	Regulation EC No. 466/2002: 0.02 mg/kg for 3-MCPD in acid-HVP and soy sauce based on 40% dry matter content
European Union	EU Cosmetic Regulations	List of substances prohibited in cosmetic products
World Health Organization	JECFA	Tolerable intake for 1,3-DCP not established due to nature of toxicity
Association of Southeast Asian Nations (ASEAN)	Cosmetic Directive	List of substances which must not form part of the composition of cosmetic products